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## AUTUMN, 1911

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**Cheyne & Burghard's Surgical Treatment.** — New Edition Shortly

**Harrington's Hygiene.** — New (4th) Edition—Just Ready See page 4

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THE

# AMERICAN JOURNAL

# OF THE MEDICAL SCIENCES

SEPTEMBER, 1911

## ORIGINAL ARTICLES

### IS THERE SPECIFIC TREATMENT FOR DIABETES MELLITUS?[1]

By Henry Sewall, Ph.D., M.D.,

PROFESSOR OF MEDICINE IN THE UNIVERSITY OF COLORADO, DENVER.

#### PRELIMINARY CONSIDERATIONS.

Vast as has become the accumulation of literature on diabetes mellitus, it is obvious that real advance in the knowldege of the disease demands still more facts. Though the observations to be detailed failed to sustain toward their conclusion the brilliant promise of therapeutic efficiency which rewarded the treatment of certain cases at the outset, it seems possible that the very failures may have value in the conception of an efficient working hypothesis.

Carbohydrates enter the stomach under a variety of complex chemical forms, but in the process of digestion and absorption they are transmuted chiefly to the relatively simple product, grape sugar or dextrose ($C_6H_{12}O_6$). When retained in the tissues, the soluble sugar appears to be reduced to a less soluble starch (glycogen), which is again converted into sugar preliminary to utilization. Sugar is said to occur normally in the human blood in a concentration of about 1 part to 1000. So essential to the metabolism of protoplasm is the carbohydrate molecule, that when this substance is not available, other foodstuffs, proteids and perhaps fats, undergo chemical transformations by which carbohydrate radicles are offered to the tissues. Whenever the proportion of sugar in the blood rises above 2 in 1000, the impermeability of the kidneys is

[1] Read before the Association of American Physicians, May 10, 1911.

overcome, dextrose passes through, and the result is glycosuria. Glycosuria is, as a rule, simply an expression of excessive concentration of sugar in the blood. The wonderful power possessed by the normal tissues of appropriating carbohydrate so as to prevent its accumulation in the circulation may be overcome experimentally by giving excessive amounts of sugar in the food. It is obvious that the physiological machinery which coördinates the metabolic activity of every living molecule with the varying supply of carbohydrate in the ration so as to provide working material for the cells while preventing an excess of sugar in the blood must be a mechanism of extraordinary complexity. *A priori*, it seems probable that lapses of efficiency in one or another part of this nutritive machinery should occasionally occur leading to a temporary glycosuria without implying any serious departure from the normal. It is also to be expected that the mechanism for carbohydrate metabolism should at times suffer from permanent defects in one or another of its parts, resulting in a more or less unmanageable tendency to the accumulation of sugar in the blood, thus giving rise to the pathological state known as diabetes mellitus. As the disorders leading to glycosuria demand for their explanation a knowledge of the normal carbohydrate metabolism of the body, diabetes is the one disease a discussion of which is attempted in every text-book on physiology. The *rationale* of the carbohydrate mechanism is made somewhat clearer by a consideration of the parallel system for the utilization of oxygen in the body. We know that the complex machinery of respiration subserves one prime double purpose, and is under the domination of one double force—the hunger of the tissues for oxygen and their intolerance of an excess of carbonic acid.

Adequate oxidation of the tissues and removal of carbonic acid presupposes the efficient coöperation of a great number of physiological events, such as the rhythmic discharge of the respiratory centre, normal elasticity of the lungs, and diffusion attributes of the air cells, sufficient contractile power of the heart and blood-vessels, and oxygen conveying power of the red corpuscles. These and many other functions regulate the procession of oxygen and carbonic acid through the body. When this process is acutely interfered with the physiological reaction is hyperpnea, in which group after group of muscles not ordinarily employed in respiration are set in action in the endeavor to satisfy the oxygen hunger of the tissues and abolish the irritation of the waste product. In an analogous way the whole metabolism of the body may be modified in diabetes in a desperate effort to give the tissues the sugar food they are denied. From a practical therapeutic standpoint our comparison is of further significance, for every physician knows that the efficient treatment of disturbances of tissue oxidation depends upon discovery of the specific erring function out of many which

may be at fault. In a similar way it is possible that the disease resulting in glycosuria may be indifferently produced by manifold different functional failures, and, as in the case of the respiratory dyscrasia, an efficient treatment can only be devised which shall correct the particular physiological function in fault. Such a conclusion brings bewildering complexity into the practical consideration of diabetes.

As the phenomena of respiration are essentially under the control of tissue metabolism, so it has become equally clear that carbohydrate in the body fulfils its function only in the molecules of the living tissue, and that the coördinate action of a considerable number of individual organs and their products is necessary to pilot the sugar absorbed through the complex route leading to its oxidation and excretion. When Claude Bernard, in 1849, produced glycosuria in a rabbit by his "piqure" experiment, puncture in a certain area of the floor of the fourth ventricle, it seemed as though the equilibrium of carbohydrate metabolism depended upon a balance between the nervous system and the liver protoplasm, for the glycosuria in question did not occur if the store of glycogen normally present in the liver was removed by starvation before the performance of the piqure. When Minkowski and von Mering, in 1889, showed that a severe and fatal form of diabetes followed the ablation of the pancreas from animals, it led to the demonstration that the pancreas furnishes to the body an internal secretion which is absolutely necessary to normal carbohydrate metabolism. Through Opie and others it has been rendered probable that this secretion is formed in the pancreas in the islands of Langerhans. The fact that extract of the adrenal body when injected into animals causes glycemia and glycosuria, and that extracts of adrenal body and pancreas mixed *in vitro* neutralize each other, led Zuelzer[2] to generalize the conclusion that the adrenal bodies and the pancreas play the part of physiological antagonists in carbohydrate metabolism, the former tending to mobilize the molecules into diffusible sugar and the latter to fix them in a more stable form in the tissues. Eppinger, Falta, and Rudinger[3] have carried on important researches upon the relations in carbohydrate metabolism of the internal secretions of the adrenals, the thyroid, the parathyroids (and chromaffin system), and the pancreas, in which it is made clear that mobilization or fixation of sugar depends more or less upon a balance between the activities of these glands. The pancreas and the thyroid, and the pancreas and the adrenals, intensely inhibit one another, while the thyroid and the adrenals are mutually stimulant in the production of glycemia. These authors made laborious determinations of the metabolism in dogs before and

[2] Deutsch. med. Woch., 1908, No. 32, S. 1380.

[3] Ueber die Wechselwirkungen der Drüsen mit innerer Sekretion, Zeitschr. f. klin. Med., 1908, 1909, etc.

after the extirpation of various glands of internal secretion. They found, for example, that in pancreas-free dogs at the height of metabolic disturbance the injection of adrenalin causes enormous increase of sugar and nitrogen elimination; whereas, like treatment in thyroid-free dogs caused no glycosuria. They hold that the glycosuria following piqure is due to a liberation of adrenal internal secretion. They conclude that while genuine diabetes has its origin in profound disturbances of equilibrium between the glandular organs regulating metabolism, the final cause of the disease remains in deepest obscurity.

Pflüger, the physiologist, in disputing the evidences for an internal secretion by the pancreas, found by experiments on frogs an important nervous connection between the duodenum and the pancreas.[4]

Severing these nerves leads to glycosuria. It is concluded that the duodenum is a peripheral regulating organ for sugar mobilization and an inhibitor of sugar formation.

Minkowski failed to confirm these results on mammals.

Pflüger holds that a nerve centre in the medulla controls the formation of diastase in the liver, and consequently regulates the rate of sugar production.

Cushing and others have shown that removal of the anterior lobe of the pituitary body is followed by metabolic disturbances in which glycosuria is one result.[5]

The ductless glands operate by internal secretions, which are absorbed by the circulation. The active agents in the secretions are known as "hormones," which "Starling defines as chemical messengers, which, formed in one organ, travel in the blood stream to other organs of the body and effect correlation between the activities of the organ of origin and the other organs on which they exert their specific effect. Such substances belong to the crystalloid rather than the colloid class; they therefore are thermostabile, and do not act as antigens when injected into the animal."

In an admirable review of the subject, Howell[6] points out that the hormone may act at least in two ways—either as a chemical stimulus, illustrated in the excitement of pancreatic secretion under the influence of secretin, or as an activator, in which role it simply develops some latent property of a chemical body, as by turning an inert proferment into an active ferment; according to Howell, "This at least would seem to be true for the hormone, of unknown nature, given off by the pancreas and concerned in the glycolysis of sugar in the organism."

However numerous may be the physiological defects which lead

[4] Quoted from Blumenthal, Deutsch. med. Woch., October 22, 1908.

[5] Johns Hopkins Hosp. Bull., May, 1910.

[6] The Chemical Regulation of the Processes of the Body by Means of Activators, Kinases, and Hormones, Science, 1910, xxxi, 93.

to glycosuria, we must believe that the fundamental nature of diabetes depends upon a disorder of tissue metabolism. As Halliburton puts it, "The difficulty in diabetes probably lies in an impairment of the capacity of the cells of the body to prepare the sugar for oxidation. In this process the sugar, or its early oxidation product, called glycuronic acid, is split into smaller molecules and ultimately leaves the body as carbonic acid and water."[7]

The current of modern observation, experiment, and speculation sets powerfully toward the conclusion that practically all the functions that we have been accustomed to define as the criteria of life in matter are carried on by protoplasm through the agency of quasi-adventitious radicles, which may join or separate from the protoplasm without altering its integrity. These radicles are known as ferments, or enzymes, for it is their fundamental peculiarity that they may cause a rearrangement of contiguous molecules without themselves being disorganized. They are essential agents in metabolism, whether of building up or breaking down. According to the view of Adami,[8] the enzyme radicle is not to be considered as a distinct molecular side chain of the cell, but rather that specific enzyme actions are a constitutional property of the living proteid molecule. There seem to be various orders of these intermediaries through which the reactions of living matter are invoked.

A conservative and accurate physiologist (Langley) maintains that the contraction of the skeletal muscle is not induced by the direct action of the motor nerve impulse, but indirectly through "receptive substances," which are interpolated between the nerve endings and the muscle, and which are not an integral part of the protoplasm, but are more or less intimately connected with it. Various drugs exert their effects by combining with the receptive substance. He believes that "nerve impulses can only cause contraction by acting on a receptive substance. . . . Curari, in combining with the receptive substances, simply prevents them (and so the contractile substance) from being influenced by nerve stimuli."[9]

It will, of course, occur to every one that the chief modern theory of immunity is founded on the assumption that a molecular intermediary, an adventitious side chain, correlates the reactions of tissue cell with the antigen.

That the muscle substance contains a glycolytic ferment has been established by a number of experimenters, and recently Ransom confirmed these results with the conclusion that, "It is possible to prepare from frozen muscle a plasma containing a ferment or ferments capable of converting glucose or glycogen into lactic acid, $CO_2$, and alcohol."[10]

[7] Diabetes Mellitus from the Physiological Standpoint, Practitioner, July, 1907, p. 1.
[8] Principles of Pathology, 2d Ed., i, 70 to 84.
[9] Jour. Physiol., 1909, xxxix, 236.
[10] A Contribution to the Study of Muscle Enzymes, Jour. Physiol., 1910, xl, 1.

The first important work in this direction was that of O. Cohnheim.[11] This author found that solutions of dextrose added to an extract of pancreas remained unchanged. A nearly equally negative result attended the mixture of dextrose with the expressed juice of muscle. But when muscle juice was added to the extract of pancreas, the mixture developed marked glycolytic powers, and considerable amounts of sugar added to it were destroyed. As this reaction occurred in a homogeneous, cell-free fluid, it must have been due to a ferment. The active substance of the pancreas withstood boiling and dissolved in alcohol, and therein resembles the active principles of the internal secretions of the adrenals and the thyroid rather than the class of ferments. It was found that the glycolytic power of the muscle-pancreas mixture was annulled by adding an excess of the pancreatic constituent. The maximum glycolytic effect was obtained when 75 grams of muscle was combined with about 0.8 gram of pancreas. Cohnheim's experiments have been repeated by a number of experimenters, some of whom have confirmed and others failed to obtain his results. To this latter group belongs Simpson,[12] a late worker on the subject.

Still more recently P. A. Levene and G. M. Meyer have submitted the problem to renewed investigation, and seem to have resolved much of its obscurity. They found, like Cohnheim, that a solution of glucose lost much of its reducing power when digested with a muscle-pancreas mixture. Nevertheless, this result does not indicate, as had been assumed, loss of sugar by oxidation, but rather a concentration of the carbohydrate molecules into osazones, which do not respond to the cupric reduction test.[13]

Building on these ideas, Zuelzer attacked the clinical problem of diabetic therapeusis.[14] He discovered that in animals made glycosuric by the exhibition of adrenalin the urine became sugar-free after the intravenous injection of an extract of pancreas. He concluded that there exists a physiological antagonism between the adrenal and the pancreatic hormones, and that diabetes was the result of the balance of power turning in favor of the former. By a method whose details are not disclosed, he made extracts from the pancreatic glands obtained from living animals at the height of digestion. In several severe cases of human diabetes, he made intravenous injections of this pancreatic extract, with the result of causing the sugar to disappear from the urine for three or four days. The patients usually suffered from a severe chill following the treatment.

W. M. Croftan describes a severe case of juvenile diabetes in which

[11] Hoppe-Seyler's Zeitschr. f. Physiol. Chemie, 1903, S. 336; 1904, S. 401; 1906, S. 253.

[12] Biochem. Jour., 1910, v. 126.

[13] On the Combined Action of Muscle Plasma and Pancreas Extract on Glucose and Maltose, Jour. Biolog. Chem., April, 1911, p. 96.

[14] Zeitschr. f. Exp. Path. u. Therapie, 1908–09, Band v, S. 307.

favorable results followed the administration by mouth of dried pancreas in capsules, followed by capsules of secretin.[15] Later, he reports success in the administration of a commercial extract of pancreas.[16]

At an earlier date A. C. Croftan[17] found great diminution of sugar excretion in diabetic patients to whom he administered a mixture of expressed muscle juice and pancreatic extract. As no further results are reported, we must conclude that later trials were unsuccessful.

## ORIGINAL WORK.

My own interest in the study of diabetes mellitus was but general in character until a little patient, a girl, aged seven years, under my care, was found to have a glycosuria which, at first manifested only in the morning urine and amenable to regulation of the diet, later became constant and unmanageable. In despair, a mode of treatment was adopted which was formulated on theoretical considerations. For a time the results were so definite and happy that I was encouraged to pursue the general plan of treatment in other cases. The therapeutic outcome in certain subjects has been of such a character as to warrant a record of the observations. These studies have been greatly extended through the cordial coöperation of certain professional colleagues, in particular Dr. Moses Kleiner and Dr. S. Ringolsky, who enjoy an exceptional clinical experience with diabetes mellitus.

At this place, also, may be expressed my deep obligations to Professor J. C. Todd, of the University of Colorado, for many scores of estimations of urea and ammonia in the urines of my patients. Cordial thanks for advice or assistance is also due to Professor W. D. Engle, of the University of Denver; Dr. P. L. Leyda, of the County Hospital, and to Dr. R. T. Woodyatt, of Rush Medical College.

## THE THERAPEUTIC EFFECTS OF MUSCLE INFUSIONS IN DIABETES MELLITUS.

In reflecting on the physiological errors involved in the establishment of diabetes, it seemed to me probable that one vital link in the pathology consisted in the lack or insufficiency of some tissue side chain, receptive body, or enzyme, by means of which the healthy tissue cells are alone enabled to appropriate the sugar in the blood. One naturally turned to the skeletal muscles as offering the principal storehouse of this glycogenic (or glycolytic) tissue

[15] Lancet, February 27, 1909, p. 607.
[16] Dublin Jour. Med. Sci., May, 1910, p. 332.
[17] New York Med. Jour., 1904, lxxix, 882.

enzyme. While it might be suspected that such an atomic group would be destroyed if operated on by the digestive apparatus, it is pertinent to recall the statement of Anderson,[18] that sensitization of an animal to a strange proteid is produced by feeding with it.

METHOD OF PREPARING THE BEEF JUICE. One pound of lean beef is ground in a sausage machine and then covered in a jar with a pint of cold water, to which thirty drops of "dilute" hydrochloric acid are added. At times, one quart of water and one dram of acid are used. The mixture stands in the ice box all night, or at room temperature for four hours, and is then strained through cheesecloth. The liquid should be drunk in the course of the day, one-half to one tumblerful at a time. The meat residue should remain nearly dry and colorless.[19]

An excellent device for expressing the juice is made by folding a strong towel once and stitching the ends round two strong sticks. The fabric should be cut so that an oblong bag is made about 11 inches wide by 6 inches deep. The moist beef is placed in this, and the sticks twisted to make pressure.

CASE I (patient of Dr. M. Kleiner, who furnished the following notes).—J. P., male, aged seventy-two years; weight, 190 pounds. Lived in Socorro, N. M. Had suffered from glycosuria for about twenty years. A sister had also suffered from diabetes. He developed diabetic cataract in both eyes during 1908. He was examined by Dr. Kleiner first in December 1909. The patient was then passing 80 to 120 ounces of urine, containing 4 to 6 per cent. of sugar. He was kept on a strict diet until May, 1910, with but slight influence on the sugar excretion. Dr. D. H. Coover refused to operate for cataract, on account of the serious condition of the patient. Dr. Kleiner placed the patient on the acid-beef infusion described above, and in two days all traces of sugar had disappeared from the urine. Dr. Coover removed the cataract from the right eye on May 2, 1910. There was slow healing, without pain or iritis. On May 30, with appropriate glasses, vision in the right eye was normal. The strict diet was discontinued, but the beef juice was partaken of for twenty days after the operation, the glycosuria remaining in abeyance and the general condition of the patient improving in every way The patient returned to his home in New Mexico, and passed from definite observation. Messages were received at intervals conveying news of his continued well-being until February, 1911, when a relapse was announced. A specimen of urine received at this time had a specific gravity of 1021, and contained a small amount of acetone and about 2 per cent. of sugar.

[18] Anaphylaxis, Johns Hopkins Hosp. Bull., July, 1910, p. 221.

[19] My friend Dr. G. B. Webb has reminded me that this is essentially the beef soup long ago advised by Dr. S. Weir Mitchell in his classic Fat and Blood in the treatment of neurasthenic cases. I have frequently employed it with satisfaction in disorders marked by malnutrition, especially tuberculosis.

CASE II (patient of Dr. M. Kleiner).—J. H. H., female, aged fifty-eight years, fairly well nourished. The patient was reckless of any rules of diet. She had had symptoms of diabetes for more than seven years. The urine contained from 3 to 6 per cent. of sugar, 50 to 90 grams in twenty-four hours, and a large amount of acetone. She was frequently prostrated with spells of great muscular weakness. During such an attack the administration of beef infusion was begun early in April, 1910. Within about three days after beginning this treatment the patient recovered her normal strength and energy, which remained with her while the treatment was continued, about two months. The glycosuria and acidosis were unrelieved by the treatment, and in June an attempt was made to improve the patient's metabolism by the administration of pancreatic extract, as in Case VII, but without success. As might have been expected, revulsion against the unpalatable mixtures caused rejection of the whole plan of treatment. The patient went from bad to worse, and died in April, 1911, in diabetic coma, complicated with uremia.

CASE III (patient of Dr. M. Kleiner).—N. H. C., female, aged forty-seven years. On a strict diet, her urine contained 5 per cent. of sugar, and she was losing weight. Beef infusion has been given, at first to the amount of 1 quart; later, 1 pint daily. Now, after three weeks, the patient is gaining weight, she feels much better, and the sugar excretion is reduced to 0.5 per cent., with a diet to which are added daily three slices of toast and a small baked potato.

CASE IV (patient of Dr. M. Kleiner.)—J., female, aged sixty-seven years. A bad case, characterized by emaciation, neuritis, and dyspnea. The urine contained a high percentage of sugar, besides albumin and casts. She has taken beef infusion on alternate days for eight weeks. There is improvement as to the pain. The urine is free from sugar, although rice with a teaspoonful of sugar daily is added to the diet.

Dr. Charles G. Duncan, of Socorro, N. M., the family physician of Case I, writes under date of March 31, 1911: "I have used the beef juice in two cases (of diabetes), and have found excellent results. One was a merchant (aged sixty-nine years), in whose urine I found large quantities of sugar. He took the beef juice . . . for two days, then waited two days before commencing again. This was kept up for two weeks, when I could not find a trace of sugar. The other case was a lawyer (aged forty-three years), who had some sugar in his urine, and the results with him were equally as good."

DISCUSSION. It is, of course, unnecessary to dwell upon the well-known fact that the clinical course of diabetes mellitus is at times apparently subject to amelioration under a great variety of

conditions and remedies which probably have no specific relation to the pathological process. It is clear that a much more profound study of the cases which have been presented would be necessary in order to establish the real meaning of the apparent therapeutic effect of the raw-beef infusion. It should be noted that at least the first four cases presented were refractory to ordinary rules of treatment. If further observation should support the hypothesis which led to the treatment—namely, that by such means the body could be furnished with a muscle enzyme capable of metabolizing sugar—an encouraging advance will have been made in the knowledge of diabetes.

Particular attention is called to the age of the half-dozen patients in the foregoing list. All were beyond middle life. Reference will be made later to other subjects, mostly younger in years, in whom little or no success attended the treatment.[20]

## THE USE OF MUSCLE INFUSIONS COMBINED WITH OR FOLLOWED BY WATERY EXTRACTS OF PANCREAS.

Pursuing the same line of argument which holds deficiency of a muscle enzyme responsible for certain cases of diabetes, is but applying current notions of physiology to assume that such an enzyme needs, like the complement of blood plasma, an amboceptor to direct its energies, or, like trypsinogen in the duodenum, an activator such as enterokinase to develop its ferment qualities. We naturally look to the internal secretion of the pancreas to furnish this intermediary body, which may, indeed, play a role quite different to those which have been indicated. In the last few years many attempts have been made to correct the diabetic dyscrasia by the administration of extracts of pancreas, and certain of the results have been very encouraging.

The present article deals with a single instructive case in which for a time there was evidence that extracts of muscle and pancreas played a coördinate action in abolishing glycosuria. That the therapeutic desideratum finally failed itself demands an explanation which is well worth seeking.

Case VII.—A. S., a girl, aged seven years. Her birth had been premature a month or more. Each year she had suffered an attack of bronchitis in the fall and spring, expecially severe when eighteen months old. The child was abnormally bright until the age of four

[20] After this paper was in type my attention was led to the brilliant lectures delivered by T. Lauder Brunton nearly forty years ago (Pathology and Treatment of Diabetes Mellitus, Brit. Med. Jour., 1874, i, 221). The author not only dwelt upon Schultzen's conception of a glycolytic ferment in the body, but deduced the conclusion that the course of diabetes might be favorably affected by feeding patients with raw beef, so as to supply deficiency in glycolytic muscle enzyme. The therapeutic application was meager and the result disappointing.

and one-half years. She was then greatly frightened, incidental to an operation for the removal of her adenoids, and for more than two years thereafter her mental brightness was less conspicuous. Glycosuria was first detected in March, 1908; she had been more or less invalided with colds all winter. The sugar at first was found only in the specimen of urine passed on rising in the morning. This was true whether the principal meal of the day was taken in the evening or at midday. For some months the glycosuria was controlled by a fairly strict diet containing no sugar and a minimum of starch. In December, 1909, she was prostrated with an infection causing enlargement of the cervical glands and serous inflammation of the middle ears. Thereafter sugar reappeared in the urine, and persisted, at least in the morning specimen, in spite of the strictest diet.

Definite observations were initiated upon the child about this time, in which I had the invaluable assistance of an intelligent mother, with her heart in the work. A rather marked icteroid hue or bronzing of the skin was apt to distinguish periods of glycosuria. The mother frequently remarked that exhibition of the beef infusion (as described below) was immediately followed by an obvious improvement in the child's spirits and brightness, and by a diminution in her abnormal appetite.

The observations in this case included a continuous record of the quantity and specific gravity of the urine secreted, with an estimate by the fermentation test of the sugar eliminated in each twenty-four hours. For a prolonged period, Professor Todd made daily estimations of the amount of urea and ammonia contained in the urine. A mere trace of acetone was constantly present in the urine, the amount apparently varying proportionately with the glycosuria. Only on one day, during an intercurrent attack of bronchitis, was it considerable.

The term "strict diet" embraced such articles as bacon, eggs, butter, cream, cabbage, tomatoes, cauliflower, lettuce, and spinach. When the patient's tolerance for carbohydrates was surpassed through the addition of toasted bread to the strict diet, the carbohydrate was withdrawn as soon as the projected experiment was concluded. Periods of a week or two were allowed to elapse between observations made to test the carbohydrate tolerance of the patient. It is worth noting that the break in carbohydrate tolerance on a given diet was marked first by the appearance of a minute quantity of sugar in the urine, but the amount rapidly increased. For obvious reasons, the observations were cut short in each case without attempting to work out the progress of this glycosuria. That the welfare of the patient did not suffer during this course of experiments is certified by the fact that whereas at the beginning her tolerance for carbohydrates was *nil*, toward the close of the series more than three ounces of bread per diem could be consumed

with impunity. For the sake of brevity, the clinical course of the case will be described merely in outline.

The patient having suffered with persistent glycosuria on a strict diet, on March 20, 1910, was begun, and continued for three weeks, the daily administration of a beef infusion, prepared essentially as described. Under this treatment the twenty-four hours' urine was occasionally free from sugar, but this at once reappeared on the addition of an ounce of bread to the diet. It may be said that with a beef infusion without acid, or in one in which the hydrochloric acid was replaced by an equivalent amount of acetic acid, the results seemed less favorable. On April 15 the daily output of sugar having ranged from *nil* to $\frac{7}{8}$ per cent., one ounce of wheat bread (toasted) was added to the ration. The glucose excretion rose to 9 to 14 grams per diem. On the 19th the acid-beef infusion was resumed, and given daily. The sugar excretion increased to 15 grams on April 22. The simple beef infusion was now abandoned, and in its place was given a mixed beef-pancreas infusion. This was made by soaking about six ounces of ground, fresh beef pancreas in one quart of water acidulated with 1 dram of dilute hydrochloric acid. After standing all night in the ice chest the mixture was strained, and to the fluid was added one pound of ground beef. After remaining four hours at room temperature the mixture was again strained and the juice was consumed by the patient in the course of twenty-four hours. The sugar excretion during the day on which the "mixed" infusion was administered reached 14.67 grams ($1\frac{5}{16}$ per cent. of the urine). On the following day, the diet remaining the same and no infusion being given, the sugar excretion fell to less than 7.6 grams, which could easily have been a fortuitous fluctuation. At the beginning of the second day, after exhibition of the mixed infusion, there was begun the administration of a pancreatic infusion. This was made by extracting about one-half pound of ground, fresh beef pancreas with one pint of water acidulated with 30 drops of dilute hydrochloric acid. From the time when the administration of the infusion of pancreas was begun the excretion of sugar ceased. The daily ounce of bread was now removed from the ration, and the urine remained sugar-free without treatment. At the same time there was improvement in the patient's general condition.

It was now important to determine whether the sugar had been driven from the urine by the pancreatic infusion alone or through some relation *in vivo* between the pancreatic infusion and the infusions which had preceded it. Accordingly, on April 28 there was added to the strict diet two ounces of bread. This caused the excretion of about $7\frac{1}{2}$ grams of glucose in the corresponding twenty-four hours. On the following day, under the same diet, a pancreatic infusion was given as before. The amount of sugar excreted rose to more than 16 grams. It was then concluded that an infusion

neither of beef, beef-pancreas, nor pancreas when given alone was capable of abolishing glycosuria, but that they might be effective when given in sequence.

The last member in this sequence was the pancreatic infusion; it was to be determined whether the efficient first member was the simple beef infusion or the mixed beef-pancreas infusion, which, according to Cohnheim, should give rise to a specific compound *in vitro*. The urine of the patient on a strict died having been sugar-free for some days, on May 15 and for three days following there were added 2 ounces of bread to the ration. Glucose to the amount of nearly 7 grams appeared the first day and rapidly increased to over 16 grams, so that on May 19 the amount of bread was reduced to 1 ounce per diem; nevertheless, the quantity of sugar still increased to over 18 grams. The administration of beef juice on the afternoon of the 19th and morning of the 20th was without effect on the glycosuria. But on the afternoon of the 20th there was given an infusion of pancreas, made by extracting 2 ounces of fresh pancreas with 1 pint of water, and the urine became sugar-free for the following twenty-four hours. Though strict diet was now resumed, a trace of sugar reappeared in the urine for three days; the diminished tolerance probably depended on a lowered resistance involved in an attack of bronchitis, for which the patient was confined to bed, and which, like frequent similar attacks, was possibly an expression of the general metabolic dyscrasia.

Without further treatment, for a period of three weeks following, with the exception of one day, the urine remained completely sugar-free, although the addition of bread to the diet was resumed and the daily amount was increased to as much as 3 ounces, which was the limit of tolerance. It appeared from the last series of observations that an established glycosuria could be abolished by a sequence of beef infusion followed by pancreatic infusion, and that, moreover, the effect of treatment was to greatly increase the range of tolerance for carbohydrates.

It was evidently of great practical moment in the therapeutic régime that an efficient substitute should be found for the fresh pancreas, which is difficult to obtain and most unpalatable. Two preparations were used with this end in view—namely, a proprietary pancreatic powder known as "Holadin," and a glycerin extract of fresh pancreas. The results were disappointing. It appeared that a glycosuria might be held in check but not abolished by administration of beef infusion followed in some hours by a series of Holadin capsules, representing 10 to 20 grains of the powder. It may be repeated that the general state of well-being of the patient appeared at its best not on the "strict diet," but when the largest amount of carbohydrate within the limit of tolerance was added thereto.

Renewed tests (June 18 and 25) were now made to verify the

favorable results previously obtained by the administration of a sequence of beef and pancreatic infusions. To my chagrin the treatment was without effect. Tolerance for carbohydrates, which had been overcome by 2 to 3 ounces of bread in the ration, was by no means increased by the treatment. Reflecting on these discordant results, it was surmised that a combination of the beef and pancreas extracts, such as had been used in the first successful experiments, might be necessary in the treatment of glycosuria. This notion was tested early in July. The addition of 3 ounces of bread to the ration caused the appearance of more than 9 grams of glucose in the urine during the same day in which a mixed infusion of beef and pancreas was given. The following day, under the same diet, with the addition of a pancreatic infusion (made by extracting for three hours 3 ounces of fresh pancreas with one pint of water acidulated with 30 drops of dilute hydrochloric acid), the urine became at once sugar-free. Here for the second time a sequence of mixed beef-pancreas infusion followed by pancreatic infusion had abolished the glycosuria.

Continuing the diet containing 3 ounces of bread per diem, sugar again appeared in the urine, but evidently the patient's tolerance had greatly increased, for whereas formerly carbohydrate tolerance had been overcome by much less than 3 ounces of bread, and when once broken the glycosuria had rapidly increased, now 3 to 4 ounces of bread caused the excretion of less than 3 grams of sugar per diem.

The child now (July 15) was placed for a time on strict diet, and the infusion treatment was repeated in preparation for a vacation in the country, where she went in a few days, in excellent condition, enjoying an ounce of bread daily with impunity. While in the country for some two months the diet had included 9 ounces of oatmeal (moist) and 2 gluten wafers daily; but the mother, who had learned to make the Fehling test for sugar, found after a time that the slightest indiscretion in diet was attended with glycosuria.

Very gradually the limits of tolerance became restricted, and in December, 1910, a small amount of sugar appeared even on a strict diet. Treatment with infusions of beef and pancreas was no longer effective. The glycosuria gradually increased, and now in April, 1911, the urine contains not only 30 to 40 grams of glucose per diem, but gives a rather strong reaction for acetone, and for the first time contains a trace of albumin.

Much might be said in the way of discussion on this case, but the results would necessarily be barren for lack of essential data. There was no obvious relation between the amounts of urea and ammonia excreted and the condition as to glycosuria.

There can be no reasonable doubt that the occasional abolishment of glycosuria was a genuine effect of the treatment. It is, of course, open to suspicion that the frequent administration of the beef infusion led to the formation of an antienzyme, yet it is hard

to reconcile such an explanation with the physiology of carnivorous animals. An extract of liver was partaken by the patient on one occasion, and work along this line seems desirable.

The report on a half-dozen other cases of diabetes treated according to the method described may be put in a few words, since the results were practically negative throughout.

Case VIII (patient of Dr. S. Ringolsky).—M., female, aged forty-one years. Had manifested occasional glycosuria since the age of twenty years. Any nervous excitement or overstrain increased the condition. The pleasant relaxation of a vacation would greatly increase her tolerance for carbohydrates. Sugar appeared in the urine when 4 to 5 ounces of bread were added to the diet, and the quantity was not decreased for the few days while the treatment was pursued.

Case IX (patient of Dr. Ringolsky).—W., female, aged about forty-eight years. Sister of the above. On a general diet she had excreted upward of 70 grams of glucose per diem, with a small amount of albumin. Her carbohydrates were limited to 3 ounces of bread; her glycosuria under treatment varied between 40 and 50 grams.

Case X (patient of Dr. Pothuisje).—Wb., female, aged fifty-nine years. On a strict diet she excreted 40 to 80 grams of sugar daily; only a slight amount of acetone. The results of treatment were negative.

Case XI.—R., male, aged about thirty years. Miner by occupation. The man was reckless in his habits; diet could not be certified to, though he was confined to bed in the county hospital. When first seen he passed urine to the quantity of about 350 fluidounces per diem, containing nearly 890 grams of sugar. Nevertheless, he claimed to feel strong and well. There was marked reaction for acetone, and Professor Engle found a maximum of 7 grains of oxybutyric acid in the first few days. Though the amount of urine and quantity of sugar excreted underwent a great diminution under treatment, the latter could not be regarded as successful. In this and the following case a profuse diarrhea was sometimes present. This was probably occasioned by the infusions. On one occasion, following diarrhea, the quantity of urine fell to 38 ounces, but the proportion of sugar rose to over 15 per cent. The man developed thromboses and general dropsy, and he died about two months after abandonment of the observations.

Case XII.—M. F., male, laborer, aged about forty-two years. Inmate of the county hospital. Not confined to bed. On a general diet he was passing 324 ounces of urine, containing nearly 912 grams of sugar, in twenty-four hours. He was treated with infusions of beef and and of "Holadin." The sugar excretion did not fall much below 300 grams per diem. Diarrhea was frequent during the observations. The patient claimed to feel much better for the treatment, but he was discharged as unimproved.

CONCLUSIONS. 1. Evidence has been presented that in a certain proportion of diabetics beyond middle age the metabolism and general symptoms may be improved and the sugar removed from the urine, at least temporarily, through the administration of an infusion of lean meat acidulated with hydrochloric acid.

2. In a single case of youthful diabetes (Case VII), though neither beef infusion nor pancreatic infusion was alone efficacious, when the one followed the other, or a mixture of the two after an interval of some hours, the urine became sugar-free. After the disease had persisted for some months this happy result could no longer be obtained. Nevertheless, the treatment, especially with the beef infusion, seemed to improve the subjective condition of the patient.

3. No good results attended the use of the commercial pancreatic powder employed.

## PASSING LEAKAGE OF THE PULMONARY VALVE.*

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INCOMPETENCE of the pulmonary valve due to organic disease is a very rare condition. Only 24 cases were noted at Guy's Hospital out of 16,000 postmortem examinations during a period of thirty-two years,[1] and 3 among 24,000 cases admitted to the medical wards of Johns Hopkins Hospital.[2] But leakage may occur much more commonly here when the flaps of the valve are normal, but the ring to which they are attached is so dilated that the normal flaps are no longer able to close the enlarged orifice. It is with this latter condition, the so-called relative incompetence, that we are here concerned.

Relative incompetence is a condition not easy to demonstrate post mortem, and many cases, no doubt, occur during life, and have been carefully described, in which the valve was found at the autopsy to be competent. R. B. Preble[3] and others have published cases in which post mortem the pulmonary valve was incompetent and would not hold water, and yet the flaps were normal in every way; but it is easy to understand that, as long as any elasticity remains in the structures about the pulmonary orifice, this ring will tend to return to its normal size as soon as the pressure stretching it is removed. Thus, a valve which has leaked freely during life may post mortem appear to be normal, and may even hold water,

* Read by title before the Association of American Physicians, May 10, 1911.

which, after all, is at almost no pressure. In the writer's opinion such temporary leakages are far from uncommon, and he notes with pleasure a recent statement of Dr. Thayer to the same effect.[4]

Relative incompetence must be due either to (*a*) an increased blood pressure within the pulmonary artery and right ventricle, or to (*b*) a want of resistance to stretching of the tissues about the orifice. The question of exactly what tissues may be here involved need not be gone into, but Hugh Stewart two years ago demonstrated before the Association of American Physician the importance of the muscular ring below the aortic orifice in preserving the integrity of that orifice, and, according to G. A. Gibson,[5] Arthur Keith has shown that a loss of tone in the muscular fibers surrounding the mouth of the pulmonary vessel allows of stretching of the fibrous tissues.

Most cases of relative incompetence of the pulmonary valve that have been described have occurred as a sequel to mitral disease, especially mitral stenosis (Graham Steel) and fibrous disease of the lungs. It has been shown by Foxwell, Stacey Wilson, and others how easily the pulmonary artery dilates under internal pressure as compared to the aorta—six times as easily, after making all allowance for the different strains under which they work—and a number of workers have further endeavored to find the amount of pressure required to dilate the pulmonary orifice so as to produce leakage there.

G. A. Gibson found that a pressure of 14½ inches of water was sufficient to cause a strong jet of water to escape through the pulmonary orifice in a sheep's heart; and in the same way a healthy human heart leaked freely at a pressure of 13 inches of water, and slightly with the pressure down to 8 inches.

We have tried a number of hearts in the same way, and on the whole with about the same results.

A bullock's pulmonary valve leaked freely at a water pressure of 6½ feet, but long before this pressure was attained the pulmonary artery was ballooned in a marked fashion. When a string was loosely put round the orifice before the pressure was raised, no leakage occurred up to nine feet.

Seven human hearts were similarly tested, and they leaked freely under pressures varying from 11 to 18 inches, and often below that amount to a slight degree.

When the pressure is gradually raised in the pulmonary artery, the vessel very easily dilates in a balloon-like manner, the sinuses of Valsalva standing out with special prominence. Then after a certain pressure is reached a jet of water escapes from a small opening which appears at the apices of the flaps of the valve. If, however, one encircles the orifice with the fingers or with a previously adjusted ligature, the pressure may be raised to several feet without any incompetence of the valve occurring. This would suggest that

the leakage is due to dilatation of the ring around the valve, and not to any distortion due to the dilating of the pulmonary artery. Under Professor Brodie's suggestion the latter experiments were done without any previous alteration of the relations of the pulmonary artery to the aorta or heart, and finally with the heart still *in situ* in the cadaver and with the pericardium unopened. These precautions did not make any appreciable difference in the results.

In none of the experiments could the aorta be made to dilate to any extent, even under a pressure of 20 feet of water, much less could the aortic valve be made to leak. There was one exception to this in the case of a heart from a boy, aged two years, who had died of whooping cough, with complicating pneumonia. Here the aorta leaked at 8 feet, and before the leakage occurred the aorta did not dilate much. The endocardium about the orifice was greatly congested, as was also the mitral valve.

As the pulmonary artery dilates so easily even under a moderate pressure (and in these experiments it is shown that after the dilatation reaches a certain point the orifice shares in it so that leakage occurs), one would expect that such dilatation and even leakage would commonly occur during life, always with the proviso that the tissues dilate during life with anything like the pressure that they do in the cadaver. The mean blood pressure in the pulmonary artery is 17.6 mm. of mercury in the cat, 12.07 mm. in the rabbit, 29.6 mm. in the dog, according to Bentner,[6] and Gibson says that "pressure in the pulmonary artery in man at the height of a vigorous systole of the right ventricle may be well above that which first causes an insufficiency." No one believes that the normal pressure ever makes a normal pulmonary valve leak, but if the pressure be raised or the tissues be relaxed, then dilatation of the artery may and can often be demonstrated to have occurred; and if the orifice shares in this stretching, leakage may be produced even to a sufficient extent to cause a murmur, such a yielding of the orifice being no doubt largely due, as Stewart and Keith have urged, to a want of tone in the muscular ring just below the orifice.

The following three cases are ones in which an evident mitral lesion so raised the pulmonary artery blood pressure that that vessel and along with it the pulmonary orifice dilated and a murmur occurred, which came and went in two of them over a period of years.

Case I.—V. A., girl, aged thirteen years. Admitted to the Victoria Hospital for Sick Children last August, suffering from pericarditis and double mitral disease, with a marked accentuation of the pulmonary second sound.

October 18 the following note was made: Pulmonary second sound still much accentuated, and is now accompanied by a distinct short murmur. This murmur is localized to an area about the size of a penny over the pulmonary area and a little below it. It is unaffected by holding the breath.

October 26. Whole precordium heaves with each pulsation of the heart. On auscultation a double mitral murmur is heard; also a pulmonary diastolic.

November 6. Mitral murmurs only present. Pulmonary second much accentuated.

November 24. Diffuse heaving pulsation of the whole precordium. In the second left interspace two pulsations are seen, of which the outer is the earlier. (The outer is probably the left auricle and the inner the dilated pulmonary artery.) Double mitral murmur present, but no diastolic murmur, with the pulmonary second. This sound is much accentuated.

CASE II.—A. P., girl, aged fifteen years. When seen on February 19, 1908, she was suffering from fever and pains in various joints. Within a few days the heart became markedly irregular and a mitral systolic murmur developed. This murmur became gradually more marked, and was present in all postures of the body. The pulmonary second was accentuated.

Two months later chorea developed. The mitral murmur was still present, and had become almost musical in character.

In June (two months later) it was noted that chorea was still evident, and the patient has developed flat foot. Mitral murmur still present, and the pulmonary second sound is markedly accentuated. A slight diastolic murmur is audible down the sternum. It is not heard in the neck. The heart is still irregular, giving an occasional quick beat. Apex is in the fifth intercostal space, just outside of the nipple line. No thrills. When patient sits up the second sound at the base becomes double and the diastolic murmur is more evident.

July 19. White blood cells, 5000. Heart again somewhat irregular. Diastolic murmur about the third left costal cartilage very evident.

October 16. Mitral systolic well marked. Pulmonary second sound much accentuated, and no murmur accompanies it in any posture. Cardiac deep dulness reaches from one-half inch beyond right of sternum to the nipple line. Apex in nipple line in the fifth space.

April 15, 1909. Feels well, and choreic movements are practically gone. Mitral systolic well marked, as is also the pulmonary second sound, which, however, is pure.

July 20, 1910. Seems quite well, but heart rather wide upon percussion, and mitral systolic murmur evident, and the pulmonary second sound is plus and accompanied by a distinct murmur. The pulse is not water-hammer in type, nor is there any bounding of the vessels in the neck.

CASE III.—Female, aged thirty years. Came on April 4, 1904, complaining of cough and shortness of breath, which had been frequent during the last few years. The note then made was that

some bronchitis is found. Cardiac apex in the fifth space in nipple line. Here, first sound is flapping and a slight presystolic murmur is audible. A diastolic bruit is heard over lower part of sternum, but no capillary or water-hammer pulse present, nor are the vessels in neck bounding.

February 19, 1905. Presystolic murmur not heard, but a slight diastolic one audible, best marked over lower part of sternum. First sound sharp at apex.

November 19, 1906. Has had one of her frequent attacks of bronchitis. Careful examination of the heart reveals a marked presystolic murmur at the apex, with a flapping first sound. Absolutely no other murmur is audible, and the second sound is pure everywhere.

February 19, 1907. Bronchitis again. Diastolic murmur again, audible about the lower part of the sternum. Apex is in nipple line, in fifth space. No murmur heard in the neck, and here the second sound is well heard and is free from impurity.

May 15. First sound flapping at apex. Second sound is pure everywhere.

These three cases are all examples of the so-called Graham Steell murmur, in that there was present well-marked mitral disease, which presumably so raised the blood pressure in the pulmonary artery as to cause from time to time leakage at the pulmonary valve. In the following cases, however, no such cause seemed to exist, and probably the leakage was more due to relaxed tissues about the pulmonary orifice than to any marked increase in the blood pressure of the pulmonary artery.

Case IV.—Mrs. C., aged thirty years. Was first seen in March, 1904, for a slight attack of appendicitis. It was then noted that she had an aortic diastolic, with well-marked second sound. Pulse was regular and not of the water-hammer type.

Two years later, in November, 1906, aortic diastolic murmur not heard. Heart sounds are all quite clear and pure.

April 5, 1907. Aortic diastolic murmur now quite evident.

Dr. Finlay, of Montreal, had previously had this patient under his care, and on my writing to him about her, he replied as follows: "I remember Mrs. C.'s case quite well. She had a soft diastolic murmur, localized about the pulmonary area, but without the compensatory enlargement or the vascular phenomena of aortic incompetence. I always felt a little uncertain as to the significance of the physical signs. I can recall another case of a diastolic aortic murmur in which at several subsequent examinations it was inaudible."

March 17. The diastolic murmur is quite evident. The heart does not appear to be enlarged.

November 13, 1910. The pulse is regular and not water-hammer in type. No throbbing in the neck. Cardiac apex is in fifth space

one inch outside of the nipple line. The sounds are clear at the apex, but down the left border of the sternum there is a slight diastolic murmur. The pulmonary second sound is accenutated. There is no murmur in the neck. The liver is of normal size.

In this case, as the notes show, both Dr. Finlay and myself presumed that the murmur was of aortic origin, but I now believe that it was an example of occasional leakage at the pulmonary orifice.

Case V.—G. W. H., aged fifty-five years; farmer. Seen last November, with Dr. Brown, of Elmwood. Suffered from pernicious anemia of at least two years' duration. His chief complaints were of weakness and dyspnea. This note was made: Pulse regular and not of water-hammer type. Cardiac apex in fifth intercostal space half an inch outside of nipple line. No epigastric or venous pulse. Right border of cardiac dulness does not reach beyond sternum. At the apex there is a slight systolic murmur, and the second sound is clear. In the aortic area the sounds are both clear, and the second is not accentuated. In the pulmonary area the second sound is much accentuated, and is accompanied by a well-marked diastolic murmur. This is best heard about the inner part of the second left intercostal space, but can be heard for about an inch below this point. It persists through all phases of respiration, but is loudest at the end of expiration, and when the breath is then held. A well-marked pulmonary systolic murmur is also present.

Of course, in this case some old organic lesion of the pulmonary valve may have been present, but this is unlikely both on account of the rarity of such and also from the fact that until two years before the patient had been in rugged health.

Diagnosis. The chief classical sign of pulmonary regurgitation is a diastolic murmur best heard on the left side of the sternum, chiefly at the end of expiration, and not audible in the vessels of the neck nor at the cardiac apex. Along with this murmur there are signs of enlargement of the right heart with displacement of the apex toward the left. There is an absence of the water-hammer pulse and of a capillary pulse. The pulmonary second sound may be weak or absent, all depending upon whether or not the diseased flaps are able to close.

In the cases, however, where the leakage is due not to organic disease, but to relative insufficiency of the valve, the first thing usually noted is the accentuation of the pulmonary second sound, which loud sound is from time to time accompanied by a murmur of the above distribution. In all the cases so far noted by the writer the murmur has not been constant, but no doubt it often is persistent, especially when due to some permanent obstructive condition farther on in the pulmonary circulation, such as mitral stenosis or pulmonary fibrosis.

Prognosis. The importance of relative insufficiency of the pulmonary valve, of course, depends upon the fundamental cause of

the leakage. Where this is mitral stenosis—probably the most common permanent antecedent of the condition—it points to a considerable obstruction at that orifice, but even then the cases may do well for years, as in Cases II and III of our series, and after several years of known pulmonary leakage seem little the worse.

Where the leakage is due rather to a relaxed condition of the tissues about the pulmonary orifice the prognosis depends entirely upon the cause of this relaxed state. Dr. Thayer[4] mentions the condition as occurring in exophthalmic goitre, and as this disease lessens, one would expect the pulmonary leakage to stop.

A pulmonary systolic murmur, the commonest of all functional bruits, probably depends upon a dilatation of the pulmonary artery, and in most cases tends to disappear. When, however, the dilatation involves the pulmonary orifice so that a diastolic leakage occurs the condition is of more import, although even yet it may completely clear up.

From the dilatable character of the pulmonary orifice, and on the other hand the resistant nature of the aortic one, it seems probable that most of the diastolic murmurs which come and go—and which are usually reported to be aortic in origin—are due to passing leakage at the pulmonary valve.

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## FURTHER CLINICAL STUDIES IN THE AUSCULTATORY METHOD OF DETERMINING BLOOD PRESSURE.[1]

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In a previous paper[2] we described in full the auscultatory method of determining blood pressure, giving details of technique, with explanation of sounds heard, and calling attention to the importance

[1] Read before the College of Physicians, May 3, 1911.
[2] Univ. Penna. Med. Bulletin, November, 1910.

of making accurate and repeated sequence readings. It may be repeated, briefly, that the method was described by Korotkow in 1906, and consists in constricting the brachial artery above the elbow in the usual manner, and then listening over the vessel at the bend of the arm. As the pressure is released a remarkable cycle will present itself. First will be heard a loud, clear-cut, snapping tone, the first phase, which is followed by a second phase, consisting of a succession of murmurs. The third phase begins with the disappearance of the murmurs and the appearance of a tone resembling in a certain degree that of the first phase, but less well marked, which soon becomes less clear in quality, or dull. At this point the fourth phase begins, and is followed by the disappearance of all sounds, the fifth phase.

In our first paper we emphasized especially the value of noting (1) tonal arrhythmias in distinguishing between functional and well compensated cardiac diseases; (2) the absence of the fifth phase in aortic insufficiency; (3) the determining of the percentage of phase length to pulse pressure, instead of measuring in millimeters only. We suggested that more attention should be devoted to the study of the relation of individual phases one to the other, instead of laying stress on one phase alone, as other observers have done. Our clinical data was insufficient on which to base accurate conclusions concerning this point, and our object was to devote a second paper to this subject.

During the past year's study we have not found it necessary to alter the conclusions reached in our first paper, so this part may be dismissed with no further discussion. Instead, we have devoted special attention to sequence reading and to their interpretation, and it is to this aspect alone that the present paper is dedicated.

A normal cycle of auscultatory phenomena consists of five phases, the systolic pressure being 130 mm. and the diastolic 85 mm. mercury. The phases are clear-cut, and bear a definite relation to the differences between the extremes of pressure.

The phases in millimeters average as follows: First phase, 14 mm.; second phase, 20 mm.; third phase, 5 mm.; fourth phase, 6 mm. Expressing it in terms of percentage based on the pulse pressure, we find since the pulse pressure equals 45 mm. that the phases have the following percentages: First, 31.1 per cent.; second, 44.4 per cent.; third, 11.1 per cent.; fourth, 13.3 per cent., or a total of 99.9 per cent.

We interpret variations in sequence readings by assuming that each phase has a physiological factor in its production in addition to the anatomical unit, and though our hypotheses have not the firm basis of an experimental control, yet clinical experience has lent some weight to their probable correctness. Our views in this regard may be set forth as follows:

1. The first phase, or tone phase, serves principally as an index as to how far the pressure must fall before the blood current can be sustained past the obstruction in the vessel caused by the cuff, at a sufficient velocity and for a sufficient duration to produce the murmur. Hence the information it affords is of negative rather than of positive value. In other words, its normal duration is of no value, but an increase or decrease in length is of importance.

2. The second, or the murmur phase, seems to be especially dependent upon cardiac effectiveness, for it is in this phase alone that the individual sounds possess a distinct element of duration, and this protracted energy, for so it must be regarded, must evidently come from the heart.

3. The third phase, or second tone phase, depends not alone on cardiac efficiency, but also on the character of the vessel wall. The more sclerotic the vessel and the greater the cardiac hypertrophy, the more favorable are the conditions for the production of a clear tone.

4. As the fourth phase, or dull tone, may be produced by a resilient vessel receiving a normal pulse shock, or by a rigid vessel receiving a weakened shock, its interpretation is more difficult, but its study quite as interesting.

If our assumptions as stated above are correct, then it is quite evident that increases in the second and third phases are dependent on cardiac strength and circulatory efficiency, while the first and the fourth phases suffer increase when there is cardiac weakness. Furthermore, in dealing with increases or decreases in any particular phase, it is important to know at the expense of what adjacent phase this has occurred. It is apparent that an increase in the third phase, for example, at the expense of the second, has not the same significance as an increase of this phase at the expense of the fourth. In the first instance the unit of cardiac strength, which we obtain by adding the lengths of the second and third phases, has not been materially changed, while in the latter it has been increased. For this reason, we recommend that the sum of the second and third phases be compared with the sum of the first and fourth phases, in order to determine whether the elements of force or those of weakness are predominating.

We reiterate the statement made in our previous paper, that, aside from the value of the persistence of the fourth phase in aortic insufficiency, little of diagnostic value has developed in regard to the length of any individual phase. Advantage has been derived, however, from studying the changes in the sequence readings, especially in decompensating cardiac lesions, as the patient improves or not. In these cases changes in the percentages of the various phases are not the only significant feature, but internal peculiarities appear. Or, to put it another way, sequence readings have a functional rather than an organic significance.

Our results uniformly show that with decompensation, or circulatory disturbances of lesser degree, the element of heart weakness (the sum of the first and fourth phases) progressively encroaches upon that of heart strength (the sum of the second and third phases). The second phase appears to be the one which is with most difficulty sustained, and often the internal variations, to be spoken of later, within the element of heart strength, precede the shortening of this element as a whole. The fourth phase, as weakness gains the ascendency, is usually the first to lengthen the element of cardiac weakness by its encroachment on the third phase, but encroachment of the first phase on the second soon adds its share to the total.

We have said that not only is the relation of the element of heart strength to that of heart weakness altered, but internal changes early appear. By internal changes we mean changes occurring in the phase itself, not as regards length, but pertaining to the relation of each individual sound to the other. Tonal arrhythmia is the most prominent of these, and simply means that there is to the ear, alternation in the intensity of individual sounds—arrhythmia of tone. We regard this form of arrhythmia as an evidence of variation in the force of individual cardiac contractions, and makes us aware of any departure from the normal before it can be discovered by palpation of the pulse or by auscultation of the heart. Tonal arrhythmias most frequently make their appearance toward the upper end of the sequence. They are first noted either as a failure of the first phase to be instituted after the first tone reaches the ear, or by a poor differentiation between the first and second phases in which tone and murmurs may alternate for a few heart beats. Internal variations in the third phase appear as the condition of cardiac weakness progresses, and are shown by alternating dull and sharp tones or by tones of different intensity. In cases when the arrhythmia is easily apparent to the ordinary method of examination, disturbance of auscultatory phenomena in the sequences is so pronounced as to be apparent even to a casual observer.

As a case of decompensation improves, the element of heart weakness gives place to the element of cardiac strength. The tonal arrhythmia and lack of differentiation between phases gradually disappear, commencing in the region of the third and fourth phases, and finally disappearing in the upper half of the sequence reading.

Our studies in the differentiation of cardiac neuroses from organic cardiac affections have not been met with results proportionate to the above detailed findings in other conditions, principally from a lack of material. We have had, however, a few striking cases which lead us to advance more strongly our belief that marked disparity in consecutive sequence readings, lack of uniformity in consecutive systolic and diastolic pressure estimations, when associated with internal variations in the various phases as shown by tonal arrhyth-

mia and poor differentiation, point strongly to the presence of a cardiac neurosis when a decompensatory cardiac lesion can be excluded.

We have chosen to illustrate the above by reporting briefly our findings in two cases:

### CARDIAC NEUROSES.

CASE I.—O. R., male, aged twenty years, dental student. Chief complaint, nervousness, palpitation, dyspnea, and precordial oppression, with general weakness. On examination the heat was apparently normal — no murmurs, no arrhythmia, and cardiac dulness normal. We reproduce two readings taken within a few minutes of each other.

| I. | | II. | |
|---|---|---|---|
| 145 | | 135 | |
| | 35.7 per cent., first phase. | | 44.4 per cent., first phase. |
| 120 | | 115 | |
| | 14.3 " second phase. | | 44.4 " second phase. |
| 110 | | 95 | |
| | 50.0 " third and fourth phases. | | 12.2 " third phase. |
| 75 | | 90 | |
| Pulse pressure, 70. | | Pulse pressure, 45. | |

Tonal arrhythmia was marked throughout the entire sequence. Note also variations in successive systolic and diastolic pressures, and complete change in character of sequences.

CASE II.—Eliz. M., aged twenty-eight years, housewife. Chief complaint, cardiac palpitation, dyspnea, indigestion, headache, and nervousness. On examination there were no signs of cardiac weakness, no murmurs, and no arrhythmia. Successive readings on the same day:

| I. | | II. | |
|---|---|---|---|
| 130 | | 117 | |
| | 28.3 per cent. | | 27 per cent. |
| 115 | | 107 | |
| | 28.3 " | | 54 " |
| 100 | | 87 | |
| | 24.5 " | | 5 " |
| 87 | | 85 | |
| | 18.9 " | | 14 " |
| 77 | | 80 | |
| Pulse pressure, 53. | | Pulse pressure, 37. | |

Tonal arrhythmias were present, but were not so marked as in Case I. Here again are to be noted marked variations in systolic, diastolic, and in pulse pressure, also in character of sequences.

### ANEMIA.

We have found the phases in anemias to be very loud and clear, and although the patient is extremely weak and relaxed, the

sequence readings assume an appearance of strength. This we ascribe to the anemic condition of the blood rather than to any intrinsic cardiac efficiency.

CASE I.—Martin B., aged thirty-eight years. Diagnosis, progressive pernicious anemia. Chief complaint, weakness and shortness of breath on exertion.

118

22 per cent., first phase.
31 " second phase.
33 " third phase.
14 " fourth phase.

60

Pulse pressure, 58.

Blood: Hemoglobin, 30 per cent.; red blood corpuscles, 1,690,000; leukocytes, 3000.

CASE II.—Margaret S., aged forty years. Diagnosis, progressive pernicious anemia. Chief complaint, edema, dyspnea, palpitation.

128

18 per cent., first and second phases.
74 " third phase.
8 " fourth phase.

43

Pulse pressure, 85.

There are marked tonal arrhythmias at the upper end of the sequence, the tones and murmurs alternating in such a way as to make accurate phase measurements impossible. The third and fourth phases were well differentiated and free from arrhythmias, despite edema, dyspnea, and palpitation

Blood: Hemoglobin, 18 per cent.; red blood corpuscles, 780,000; leukocytes, 6600.

## POLYCYTHEMIA.

Since in anemia the phases are loud and clear and well marked, by analogy it might be anticipated that in polycythemia the opposite should obtain. Heretofore there has been no such case studied, but through the kindness of Dr. Klaer we have had the opportunity of making blood-pressure estimations in such a condition.

William B., aged about forty-two years. Diagnosis, polycythemia.

| I. | | II. | |
|---|---|---|---|
| 128 | December 23, 1910. No phases obtainable. All sounds distant and muffled. | 114 | January 3, 1911. No phases obtainable. All sounds weak and muffled. |
| 105 | Pulse pressure, 23. | 93 | Pulse pressure, 21. |

Blood: Hemoglobin, 100 to 110 per cent.; red blood corpuscles, 8,000,000 to 11,000,000.

Our surmise was correct, for there was no differentiation of the phases possible, and the sounds had a "sticky" quality which defies description. This is the first case of polycythemia reported in literature studied with the auscultatory method of determining blood pressure, and exhibits the features which some German observers contended would accompany such a condition.

We have been interested in charting in a graphic form the blood-pressure results obtained in various conditions. These charts are based on the percentage length of individual phases to the pulse pressure. The first one represents a normal sequence in a young subject with a healthy heart and soft arteries, and shows graphically the ratio of cardiac strength to cardiac weakness, 55.5 to 44.4. We abbreviate as follows: Cardiac strength (C. S.); cardiac weakness (C. W.).

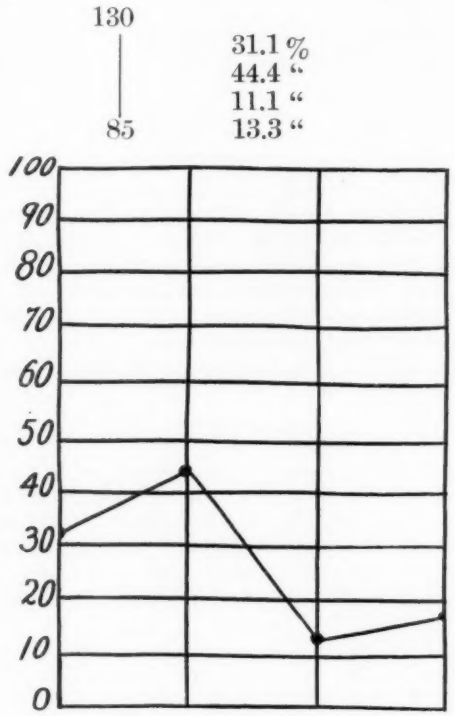


CHART I.—Normal sequence.

Considering next the pathological conditions and attempting to chart them in like form, we encountered some very interesting things.

MITRAL STENOSIS.

On admission the patient was slightly dyspneic, with duskiness of lips and hands. The chart shows graphically the elements of cardiac strength to be below those of cardiac weakness. C. S. : C. W. = 42 : 58.

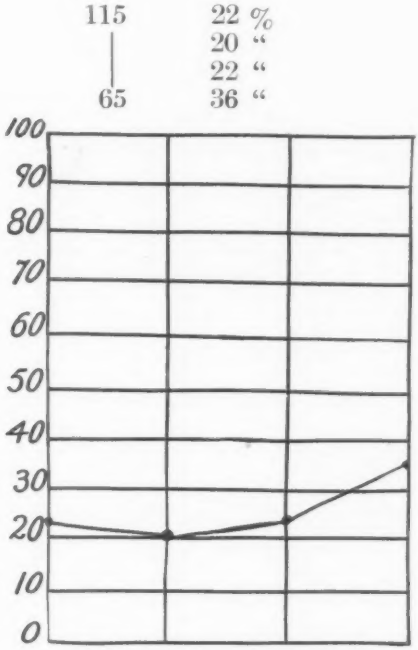


CHART II.—Mitral stenosis.

The next week on treatment there was a distinct change in the blood pressure readings. Here in the appended Chart III is well shown the increase in the lengths of the second and third phases, with a corresponding decrease in the first and fourth. The ratio of cardiac strength to cardiac weakness is 72.5 to 27.6, and the patient was subjectively and objectively improved.

MITRAL REGURGITATION.

CASE I.—The patient, a man, aged forty-nine years, came to the dispensary complaining of cough, palpitation of heart, and dyspnea on slightest exertion. There was dilatation of the right and left ventricle, with extrasystoles and marked arrhythmia. Tricuspid insufficiency, with pulsating liver.

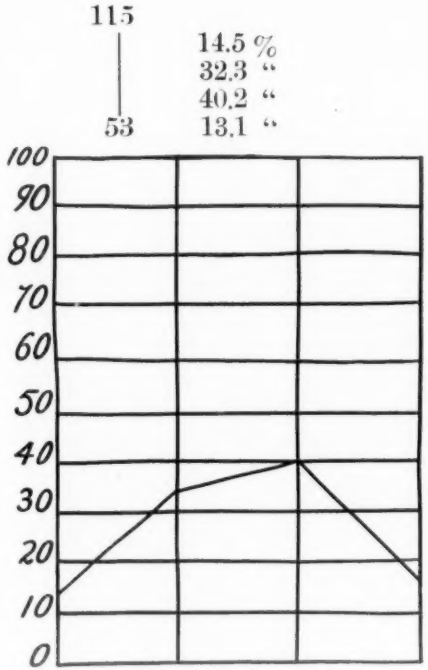


CHART III.—Mitral stenosis.

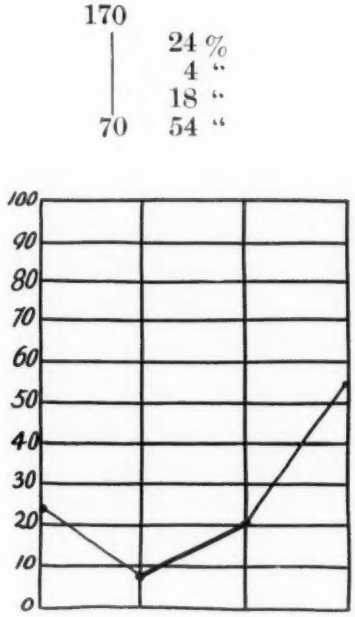


CHART IV.—Mitral regurgitation.

There were time and tonal arrhythmias, and this factor was obtained: C. S. : C. W. = 22 : 78 (Chart IV). Later readings with improvement of the patient developed the following curve:

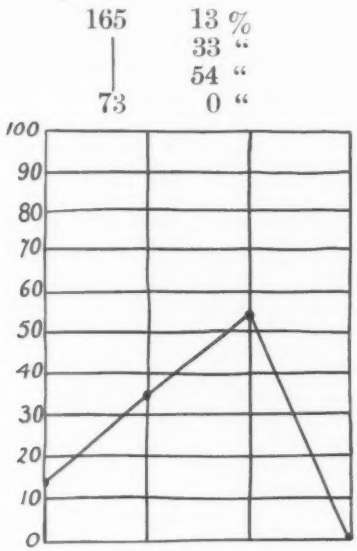


CHART V.—Mitral regurgitation.

There were no tonal arrhythmias, and C. S. : C. W. = 87 : 13. No fourth phase was obtainable.

CASE II.—On admission the patient, a man, aged eighty-three years, had failing compensation secondary to mitral insufficiency, with dilatation of right and left heart. Marked arteriosclerosis.

On admission C. S. was below C. W., there was marked tonal arrhythmia, and the phases could not be differentiated. Subjective and objective improvement were noted, and with this the two curves became divergent, the C. S. remaining above C. W.

The sequence reading is herewith appended, and bears a striking resemblance to the foregoing case, when his heart became compensated. The increase in the length of the third phase is explained by arteriosclerosis in both cases, but in Case II the arteriosclerosis was very marked.

The appended chart represents the curve of the cardiac condition under treatment. The continuous lines represent the cardiac strength and the dotted lines the weakness.

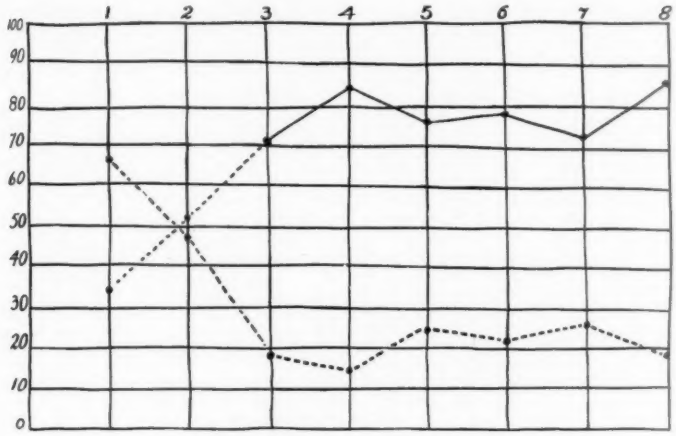


CHART VI.—Mitral regurgitation.

AORTIC INSUFFICIENCY.

On admission the blood-pressure reading was:

188
0

15 %
3 " C. S. : C. W. = 50 : 41
56 "
26 "

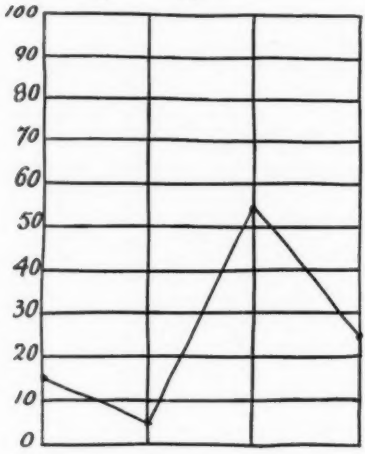


CHART VII.—Aortic regurgitation. On admission compensation poor.

The pathognomonic sign of aortic insufficiency—namely, absence of fifth phase—was seen.

On account of high blood pressure, we wished to try the effect of nitrites on the circulation, with what result is graphically seen in the following chart:

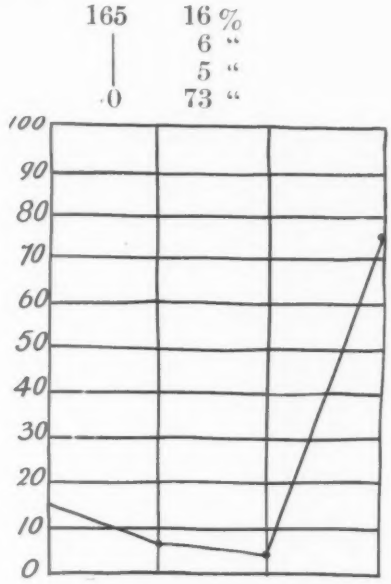


CHART VIII.—Aortic regurgitation. Effects of nitrites prior to recuperation of heart muscle.

The blood pressure was reduced, but withal there was a falling off of C. S., so that the ratio now was C. S. : C. W. = 11 : 89.

The medication was immediately discontinued, and with fair compensation there was a return of the ascendency of C. S. over C. W.

On this day blood pressure showed the figures represented in Chart IX.

The course of the disease is well shown by Chart X, in which we have depicted the cardiac strength (solid line) and the cardiac weakness (dotted line).

1. On admission (Chart VII).
2. Effect of nitrite (Chart VIII).
3. Condition of circulation improved.
4. Improvement more marked (Chart IX shows this sequence), and the patient, contrary to our advice, returned to work (ten hours on his feet as motorman).

5. As a result of the work the patient's condition became much worse, and he had to quit. The man was ill with dyspnea and marked edema, and was advised to enter the hospital. Refusing to do this, he left the dispensary and never returned.

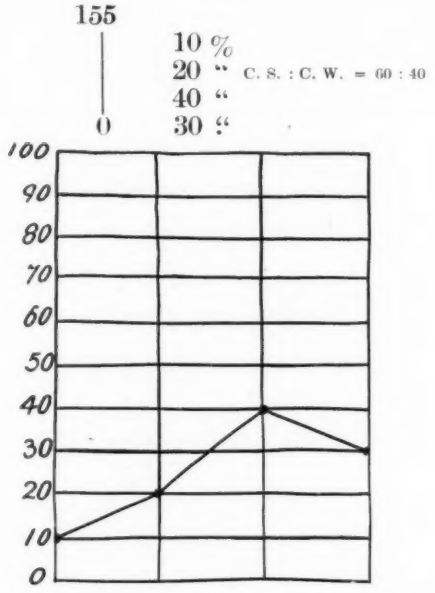


CHART IX.—Aortic regurgitation. Compensation fair, heart muscle in better condition.

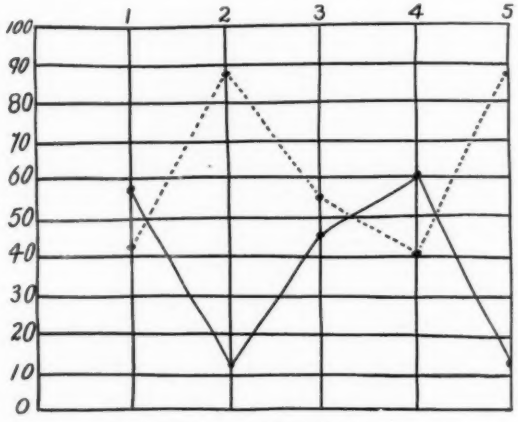


CHART X.—Aortic regurgitation.

240 — 135

14 %
33 "
9 " C. S. : C. W. = 42 : 57
43 "

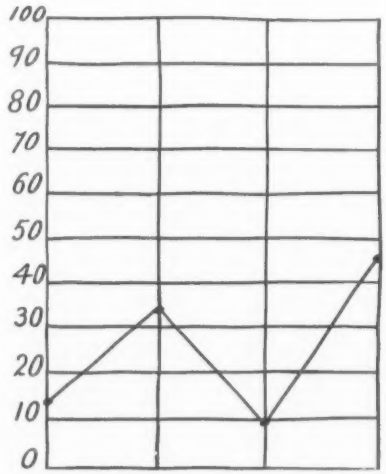


CHART XI.—Arteriosclerosis. Uncompensated single sequence.

225 — 130

7.3 %
24.2 "
63.1 " C. S. : C. W. = 87.3 : 12.5
5.2 "

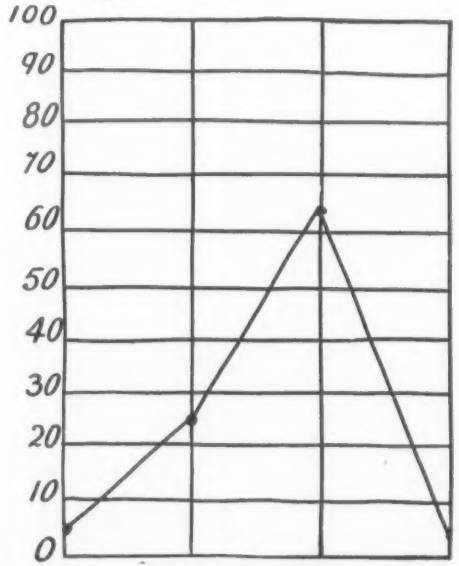


CHART XII.—Arteriosclerosis. Compensated single sequence.

ARTERIOSCLEROSIS.

This patient, a man, aged sixty-eight years, was referred to us from the eye dispensary, where he had gone for dimness of vision of both eyes. There was an enormous enlargement of the heart to the left and a moderate hypertrophy to the right. The arteries were markedly sclerosed, and later examination revealed a chronic diffuse nephritis with induration.

On admission the functional activity of the heart was not at its best, and for want of a better term we have said the heart was decompensated.

In arteriosclerosis the third phase is long, but here, owing to cardiac decompensation, it has become short. (Chart XI.)

When compensation set in the curve changes, and here the characteristic lengthening of the third phase is seen (Chart XII).

The course of the disease is well represented by Chart XIII.

The indication which we sought to meet was the high blood pressure, and, in addition to rest, bland diet, etc., we placed him on large doses of sodium nitrite and nitroglycerin. The first visit we were unable to determine his blood pressure, it being 260+. There was a gradual fall from this figure to No. 7 (Chart XIII), when the pressure reading was:

| | | |
|---|---|---|
| 202 | | |
| 183 | 20 per cent. | |
| 147 | 38 " | C. S. : C. W. = 56 : 44. |
| 130 | 18 " | |
| 108 | 24 " | |

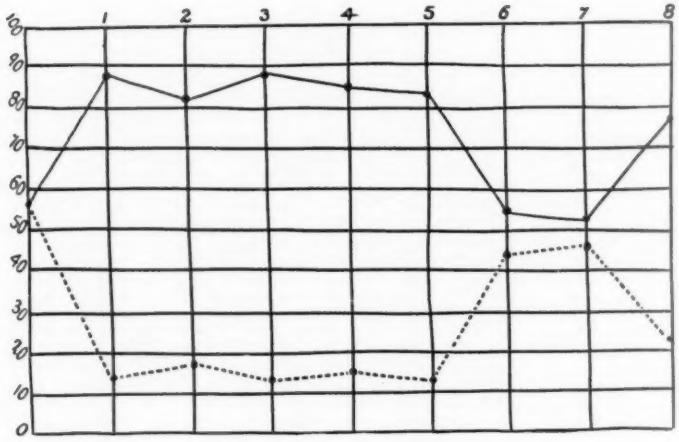


CHART XIII.—Arteriosclerosis.

On this day, as seen on Chart XIII, the two lines approximate, and the patient felt weak, "played out," no ambition for physical or mental effort, and the task of coming to the dispensary had depressed him more than at any other time. The nitrites were immediately discontinued, and no medication was given, and the next week (No. 8) the patient was improved and the blood pressure had gone up slightly.

No. 8.

209

17 per cent.
28 "
50 "
5 "

C. S. : C. W. = 78 : 22.

116

We cannot refrain at this point from emphasizing the importance of controlling, by blood-pressure estimations, medication given to combat high pressure. In cases of hypertension the cardiovascular system has readjusted itself to altered conditions, and the normal, for them, is a pressure far exceeding the normal as given by us in Chart I. The injurious effect, or what would ultimately have been an injurious effect, is shown graphically in Charts X and XII, when, with the reduction of blood pressure, cardiac function was materially impaired.

In the case of the patient from whom Charts XI, XII, and XIII were plotted, the blood pressure was normal at about 220, or, in any case, subjectively he was best with that pressure, and with that pressure the factor was obtained of C. S. : C. W. = 87.3 : 12.5. When the pressure fell below that point, the ratio of C. S. to C. W. became altered in favor of the latter, and the patient felt what is best described by the German word "Matt," and we believe he was on the verge of a vasomotor collapse, and that to have reduced the pressure still farther would have been accompanied by serious consequences. The point is not sufficiently recognized that, owing to the gradual increase of blood pressure, each individual readjusts his cardiovascular physiology to compensate this, and the physiological limit is now, not 130, but may be as high as 220, as in our case. To reduce pressure below this new physiological limit is not only not indicated, but bad therapy, and hence we reiterate that with cardiac depressor drugs, or with vasodilator measures, blood pressure must be constantly watched with the sphygmomanometer.

### CHRONIC NEPHRITIS.

Charts XIV, XV, and XVI represent three successive sequences taken on different days in a patient showing no circulatory symptoms. They illustrate the effect of the anemia in lengthening the second

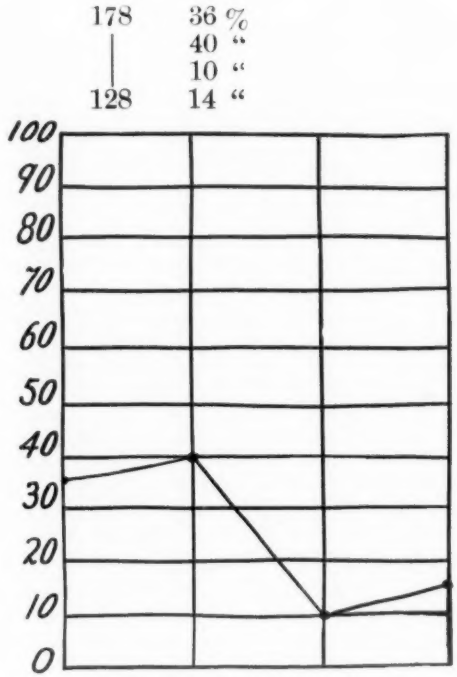


CHART XIV.—Chronic nephritis (anemia).

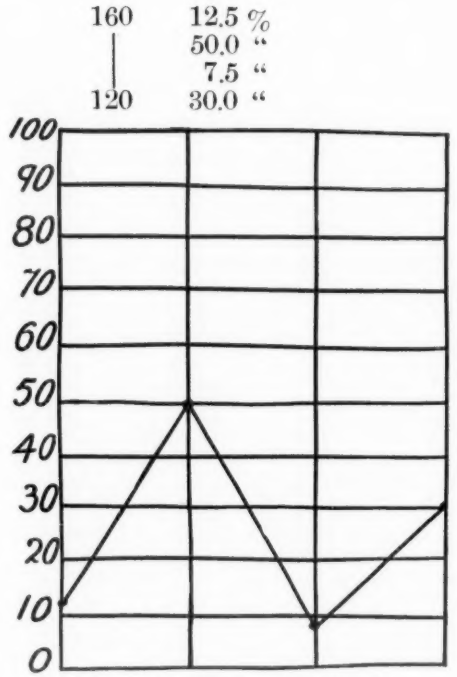


CHART XV.—Chronic nephritis (anemia).

phase. We said above that arteriosclerosis was accompanied by a particularly loud, long, third phase, and it is of interest to note here that despite some arteriosclerosis the second phase is longer than the third, due, we think, to the good functional state of the heart and to the anemia.

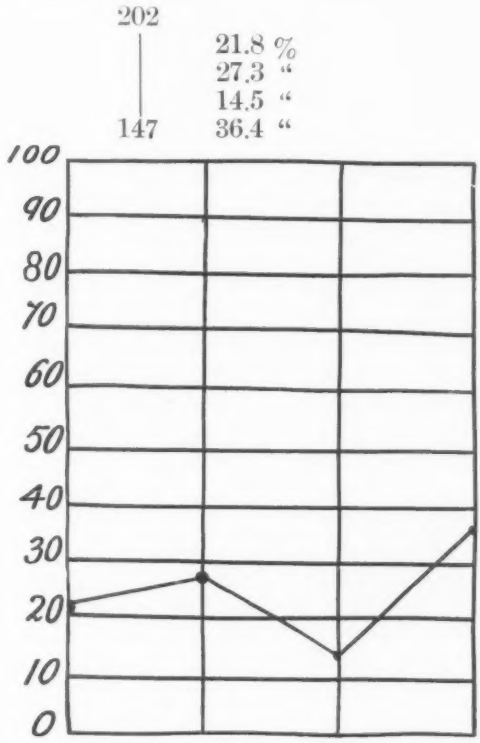


CHART XVI.—Chronic nephritis (anemia).

MYOCARDITIS.

In cases of organic disease of the heart, where the function is impaired, as in myocarditis, the sequence readings may show no phases, or one phase may be lacking, usually the second or third, and with these changes tonal arrhythmias are quite easily detected. In distinction to the functional disturbances without any apparent organic lesion, the so-called cardiac neuroses (see above), there is no variation in successive systolic and diastolic readings, which we believe to be characteristic of the neuroses.

CASE I.—Katharine D., aged fifty-five years.

170
160
A few murmurs alternating with tones. The tones were weak, but fairly clear in quality.
110

CASE II.—John W., aged sixty-three years.

157
No second phase.
90
85

Arrhythmia as to time, none as to intensity.

CASE III.—E., male, aged twenty-five years.

110
100 Murmurs and tones alternating. No third phase.
80
65

We feel that the auscultatory method of determining blood pressure has a large field of usefulness, and that by observing the phases and their relation to one another in each sequence reading, much may be learned of diagnostic, therapeutic, and prognostic interest.

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## DIFFUSE SELECTIVE SCLEROSIS OF THE SUPERFICIAL VEINS.

BY HARLOW BROOKS, M.D.,

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THE selective tendency for definite systems or groups of trunks which is manifested in arteriosclerosis has long been recognized, and usually the change is most marked or sometimes even limited to a certain group of vessels. In some instances this selection seems to be determined by the nature of the exercise or occupation; thus, for example, we expect it to be most evident in the peripheral trunks in athletic or physical workers, and more advanced in the vessels of the central nervous viscera in those chiefly engrossed with nervous problems, even though the probable direct etiological factor be such a general one as a toxemia or syphilis. In other cases, however, the selective tendency appears to be due to the character of the cause or the route of its excretion; for example, in alcoholism we all recognize the frequency of involvement of the renal and hepatic vessels.

No less frequently, in my opinion, only less obviously, is this selective tendency shown in sclerosis of the veins. It is often rela-

tively quite as evident here, and it occasionally becomes even more suggestive and striking, since the veins are usually much less liable than the arteries to this type of lesion. This fact is most likely chiefly due to the lesser pressure to which these trunks are habitualy subjected. This assumption is, I think, quite warranted by the relatively more frequent occurrence of venous sclerosis in the various long trunks, notably in those of the lower extremities, which during the erect posture of the body have a far greater pressure to sustain than the veins of other distributions, and are associated during exercise with constant mechanical shocks, which probably cause minor traumatic changes in the thin walls of the venous trunks.

I believe that the following case of selective venous sclerosis is of peculiar interest, since it occurred in an individual very young for the development of any form of vascular sclerosis, and especially because of the definite selective tendency manifested in this instance for the superficial veins of the peripheral distribution, with no evidence of other venous or of arterial involvement.

The patient was a well-formed, rather sparely built boy, aged eighteen years. He was born in Austria, but for the last three years had lived in and around New York.

He entered the City Hospital with the chief complaint of pain in the left leg and thigh, so severe that he was unable to walk. The veins were stated to be hard and swollen.

The family history was practically negative; there was no history of ancestral alcoholism, gout, or syphilis.

The patient was a waiter by occupation, but had worked at this but a little over a year, previous to which time he had no regular work, but attended school most of the time. He had never done heavy physical exercise and had never been inclined toward sports involving this. He believed that he was healthy as a child and remembered no time when he was confined to bed on account of illness, except for a slight attack of "pneumonia" and for several mild attacks of tonsilitis and pharyngitis. There was specifically no history of rheumatism, gout, malaria, typhoid, or of previous venous disturbances. Of late he had used alcohol moderately, perhaps a couple of glasses of beer daily.

About one month ago, after a night spent in the society of a vigorous young woman, the patient noticed some pain and swelling with local redness on the inner side of the left leg. He went on working, and for three days paid no particular attention to it, when he found that the swelling extended and the pain became so intense that he was forced to seek aid, having first attempted relief by rubbing the parts with various medicaments, such as vaseline and alcohol. No relief followed this local treatment, and after the third day he entered my service at the City Hospital.

On examination, he was found to show a complete thrombosis of the left internal saphenous vein, extending from 8 cm. below

Poupart's ligament down to the ankle. The course of the vein was marked by a hard cord bordered on either side by an indurated and tender red band. Considerable edema, especially about the ankle, was present and he suffered exquisite pain, particularly on movement. A circular point of sharply localized bluish discoloration was found over the vein just below the knee-joint, evidently a gangrenous area. Aside from this, no lesions of importance were demonstrable on physical examination except that the superficial veins of the entire body, notably those of the extremities, were prominent and palpably thickened. The hands were constantly cyanosed, and if allowed to hang down, soon became edematous. Moderate exertion caused facial cyanosis of a peculiar mottled quality; areas of edema also occasionally developed over the face.

Examination of the heart, which was conducted with particular care and on many occasions, revealed nothing of importance; it was regular, no murmurs were present, and no disturbances of rhythm. The pulse rate varied, according to posture, condition of excitement, or after exercise, from 82 to 100 per minute, and no arterial thickening could be made out. No change in the retinal vessels, either veins or arteries, was apparent.

The blood pressure chart showed on admission a systolic pressure of 120 mm. Hg, which subsequently went up while the patient was still in bed to 140 mm., slowly falling under treatment to 110 mm. Hg. The temperature varied while under observation from 97° to 99.2°, being mostly at the normal level.

The urine was entirely normal throughout, and no conditions suggestive of either renal or hepatic disease were found.

The blood examinations showed little of importance and varied but little from the condition first found, which was as follows: Hemoglobin, 70; red blood corpuscles, 5,456,000 per c.mm.; white blood corpuscles, 7200 per c.mm. Differential leukocyte count: Polynuclear neutrophiles, 68.5 per cent.; large lymphocytes, 1 per cent.; eosinophiles, 1 per cent.; small lymphocytes, 21.5 per cent.; transitionals, 7.5 per cent.; basophiles, 0.5 per cent.

The coagulation time, as determined by the Biffi-Brooks instrument, showed considerable reduction, varying from two and one-half to three minutes.

Blood cultures were negative.

The Wassermann reaction, at this time little understood, was not tried.

There were absolutely no signs or symptoms suggesting faulty deep visceral action of any kind.

The patient, greatly to his discomfiture, was kept in bed. The leg was wrapped in cotton moistened with 33 per cent. alcohol and citric acid, and potassium iodide was administered internally.

Shortly after entering the hospital the gangrenous spot sloughed out, leaving a circular perforation 7 mm. in diameter and 1 cm.

deep, this quickly granulated up and rapid absorption of the clot in the thrombosed vein took place, although up to the time of his discharge circulation through it was not fully reëstablished. The patient gained some two or three pounds in weight while under treatment, and left the hospital after three weeks, walking, and, aside from the thickened veins, apparently well.

Briefly, the chief features presented by this case were, a diffuse, isolated sclerosis of the superficial veins, with phlebitis and thrombosis of one.

This condition is remarkable in that the sclerosis was apparently limited to the superficial veins, and was certainly relatively much more marked in them than in the other veins or the arteries. Although the coagulation time of the blood was considerably reduced, and in accordance with experiments conducted by Crowell and myself,[1] I believe that this favored the thrombosis; the chief factor back of it was the markedly altered, and in this instance clearly sclerotic alteration in the walls of the veins.

With no other evidence at hand, and the case was most carefully studied in all its aspects, it seems most likely that this selective venous sclerosis was induced by syphilitic infection either congenital or early contracted. The very early age of the patient and his apparent freedom from other lesions, which might be considered as causative in nature, direct one by exclusion toward this diagnosis, although no direct evidence of its accuracy can be advanced. We know that in syphilitic arteritis, a condition much more frequent and much more fully studied, this selective tendency toward the involvement of certain specific vascular distributions has been well established, and in my opinion it may with equal force be directed to the explanation of this unusual instance of diffuse superficial venous sclerosis occurring in youth.

## RETROBULBAR NEURITIS AS AN EXACT DIAGNOSTIC SIGN OF CERTAIN TUMORS AND ABSCESSES IN THE FRONTAL LOBES.

By Foster Kennedy, M.D., B.Ch. (Queen's),

late resident medical officer, national hospital, queen square, london; chief of neurological clinic and instructor in neurology, cornell university medical college; chief of clinic, neurological institute, new york.

The diagnosis of tumor and abscess formation in the frontal lobes has for long been a matter of very considerable difficulty, owing to the paucity of definitely known centres in these areas;

[1] Journal of Experimental Medicine, 1908, vol. x, No. 2.

we have been compelled to look for our main guidance to the effects of pressure exerted backward on either the pyramidal tracts or their cortical origins; and to the existence of some abnormality of mental state as a more or less confirmatory factor. It will readily be seen that, valuable as these phenomena may be, when judiciously and skilfully considered, they may be at times but sorry sign-posts, and any concrete indication by which we may be able to augment them must be welcomed as a valuable addition to our ability to diagnosticate and treat these conditions.

It is the purpose of this paper to consider, in some detail, the various subjective and objective signs in a series of 6 cases of expanding lesion of the frontal lobes. In 5 of these the accuracy of the diagnosis was proved by operation. In the sixth, a palliative decompression operation only was attempted, in consequence of which procedure the tumor was not seen; nevertheless, the propriety of including it in this series will not be questioned when it is realized how completely it coincides in symptomatology with its fellows.

The 6 cases to be considered in this paper are set thus in series, for the reason that, in each, there is shown a symptom complex which, if looked for, is easily discoverable, and which is decisively diagnostic, in that it cannot possibly be simulated by any lesion failing to exert pressure on the inferior surface of one or other frontal lobe.

This sign to which I wish to draw attention is the occurrence of true retrobulbar neuritis with the formation of a central scotoma and primary optic atrophy on the side of the lesion, together with concomitant papilledema in the opposite eye.

One may say that if there be no doubt that a given patient has a brain tumor, and if that patient develops a unilateral retrobulbar neuritis, then it is certain that the tumor is situated in the lower part of the frontal lobe on the same side as that on which the retrobulbar neuritis and primary optic atrophy have occurred.

Before discussing the mode of production of these phenomena, it may be well, in a few sentences, to consider some important points in the structure and pathology of the optic nerves. Both developmentally and anatomically they form a part of the central nervous system; their constituent fibers take origin in the ganglion cells of the retina; like other central fibers, they are without primitive sheaths, and in consequence, when once destroyed, they are incapable of regeneration. The sheathless fibers maintain fairly definite relative positions in their course through the optic nerves, and it has been found that fibers originating in the macular region of the retina lie as a wedge-shaped bundle toward the outer side of the nerve, the apex of the wedge being directed mesially while the base is covered completely by fibers coming from retinal areas other than the macula.

This macular bundle subserves central vision; physiologically

more delicate than its fellows, its structure presumably is proportionately more fragile; the result being that direct pressure on the optic nerve has, as a first consequence, a deterioration of function, and later, a primary atrophy of the macular fibers with loss of central vision; and this in spite of the fact that the grosser strands retain functional activity, though subjected by their peripheral position to more immediate and direct trauma.

The sequence of events just described is that which takes place when, from the earliest inception of disease, one or other optic nerve be directly subjected to pressure. If, however, the expanding lesion be situated in the substance of the frontal lobe, not implicating at first the underlying optic nerve, but producing a general rise of intracranial pressure, there will be brought about a bilateral papilledema without central scotoma, or loss of visual acuity.

The tumor or abscess expands until at last it presses directly on the upper surface of the ipsolateral optic nerve. The following phenomena will then result: The papilla contralateral to the tumor will remain edematous and visual acuity in that eye will, for a considerable time, remain good. In the ipsolateral eye edema will rapidly subside and visual acuity will quickly diminish, a central or paracentral scotoma will develop, and in a few days time, well-marked temporal pallor will be seen opthalmoscopically, an expression of atrophy, which, at a later period, will be observed in all four quadrants of the disk.

In order properly to understand the mechanism of these occurrences, it is necessary to review the methods by which a general rise of intracranial pressure results in optic neuritis, or, to use the much better term suggested by de Schweinitz, papilledema. There have been many theories on this subject. Hughlings Jackson and Brown-Séquard put forward a somewhat vague hypothesis which has been called the "reflex irritation" theory, which alleged the papillary changes to be the result of certain nutritive alterations in the walls of the intracranial bloodvessels produced by the presence of a foreign body in the cerebral substance. By others, a slight, basal meningitis has been thought to be constantly co-existent with neoplasms, from which meningitis, an inflammatory process, descends along the optic nerve coverings to find its ultimate expression as a papillary neuritis. A third theory argues for an intense cerebral edema communicated directly to the papilla of the trunk of the optic nerve.

It is beyond the scope of this paper to discuss the merits of these various contentions, all of which find some champion even at the present day. The explanation which most fully satisfies conditions is supported by sound evidence at once anatomical, pathological, and therapeutic, and may be designated the "mechanical" theory of papilledema.

In support of this view the following facts may be cited: (1)

The space between the optic nerve and its sheath is directly continuous with the intermeningeal spaces about the brain. (2) When intracranial pressure is raised, an excess of cerebrospinal fluid is forced into the intervaginal spaces of the optic nerves; a resultant edema is thus created around the nerve heads. This distention of the intervaginal sheaths may easily be demonstrated by autopsy in cases where papilledema has been seen clinically. (3) The occurrence or non-occurrence of papilledema in cases where intracranial pressure is raised is dependent in the highest degree upon the formation of the eyeball; in hypermetropic and emmetropic eyes the ocular ending of the vaginal space is directed sharply *toward*, and in myopic eyes *away from*, the optic nerve, an arrangement which, in the latter condition, results in an infiltration of the fluid contained in the sheath through the sclera, while in the former the nerve head becomes speedily edematous. (4) Decompression operations producing a diminution in an increased intracranial pressure are followed by a corresponding diminution in the degree of papilledema present.

These considerations make clear the method by which a constriction placed on an optic nerve in which papilledema has already occurred is capable of abolishing that papilledema and substituting for it what may accurately be termed a primary optic atrophy.

The optic nerve lying below the frontal tumor or abscess, together with its fellow on the opposite side, is in a condition of papilledema the result of generally raised intracranial pressure. As we have just seen, the nerve fibers are intact and the sheaths are distended with fluid, the papillæ, in consequence, being swollen and edematous. The superjacent foreign body grows until it at last presses on one of the optic nerves, the sheath of which becomes constricted so that the passage of fluid from the intracranial cavity to the nerve head is prevented. The excess of papillary fluid and that contained in the optic nerve sheath distal to the constriction then disappears by filtration and absorption; that is, the opthalmoscopic appearances of papilledema vanish and, as the pressure on the optic nerve becomes more pronounced, the various phenomena associated with retrobulbar neuritis become manifest.

Owing to the proximity of the olfactory bulbs to the optic nerves, we would expect that trauma to the latter would inevitably produce damage to the former, and, as will be seen in the following cases, depression or loss of the sense of smell is practically always found on the side on which retrobulbar neuritic atrophy has occurred. It is not intended to discuss in detail the other signs of frontal lobe lesions which were present in these cases; the mental state in which a trivial and meaningless jocosity predominates, the tremor in the hand ipsolateral to the tumor, nor the signs of gradual compression of the pyramidal tracts going to the opposite side of the body. These things have been fully dealt with by other observers, and their

presence will be indicated in the case reports. Nor is it wished to becloud the diagnostic importance of the sign which has just been discussed and which is the main purpose of this paper.

The first case is that of a woman, aged thirty-seven years, who, in September, 1908, was admitted to the National Hospital, Queen Square, London, to the service of Sir William Gowers, who has kindly allowed me to make use of my old notes.

The history was briefly as follows: For many years she had been subject to fainting attacks of more or less prolonged duration. In all other respects her previous health had been good. In October, 1906, she began to suffer from headaches of increasing severity, with marked fatigue. One evening, after considerable exertion, she fainted and remained unconscious for two hours, after which she had a severe vomiting attack, which lasted for a whole night.

During 1907, headache, nausea, and vomiting increased, and in June of the following year she began to have transient blurring of vision in the left eye, and later some weakness slowly developed in the left arm and leg. She came into the hospital in September, 1908. Her mental condition was normal. Nutrition was good. The sense of smell was completely absent on the left side, while on the right, though at first normal, in the course of six weeks it became lost.

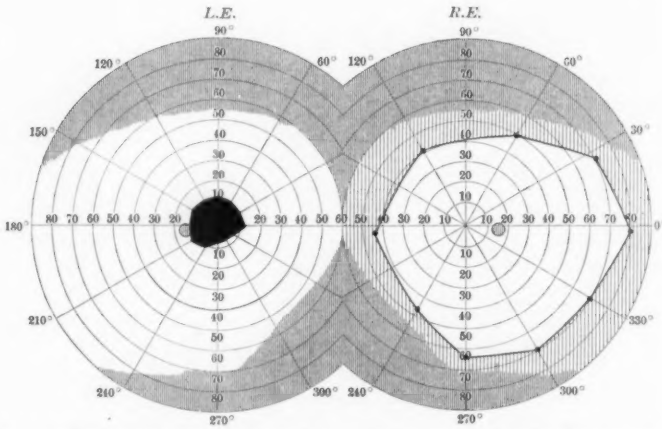
The left optic disk was clear, its edges were sharply outlined, the physiological pit was not filled in, and the vessels were rather below normal in size. Its color was grayish, particularly in the temporal portion of the disk. The right disk offered a striking contrast, being markedly edematous to the extent of 5 diopters; the edges were completely obscured, the veins were enlarged, and the amount of retinal exudate was considerable. Visual acuity in the left eye was markedly depressed. Jaeger test types could not be read, and under observation, vision rapidly retrogressed, so that light perception was but dimly retained.

The visual acuity of the right eye was at no time less than normal, despite the high degree of papilledema present. The visual fields were as shown in Fig. 1, that is, the left eye showed the presence of a central scotoma complete for white and for colors up to 10°, while in the right there was a mild degree of general concentric contraction.

The pupils were equal, both acted briskly to light, but the contraction of the left was not sustained. It quickly dilated again, despite the maintenance of illumination, a phenomenon so characteristic that it has been called by the late Mr. Marcus Gunn "the retrobulbar reaction." The other cranial nerves were normal. There was considerable diminution in the power of the left arm and hand, and to a less extent in the left leg as well. The deep reflexes on the left side were increased; the left abdominal reflexes were diminished; the left plantar reflex was never obtained, while that

on the right was always of the flexor type. At no time was there any change in sensation.

An effort to remove the tumor was made by Sir Victor Horsley in October. The patient, however, died shortly after the initial decompression operation had been completed. On autopsy, a a subfrontal indurated endothelioma was revealed, its origin having been taken from the dura mater over the crista galli. The growth compressed but did not infiltrate the cerebral tissue, and measured in circumference about seven inches; in anteroposterior diameter, two and one-half inches, and from side to side two and five-eighths inches. It extended farther backward on the right than on the left side, by which circumstance the production of the left-sided paresis became plain. The left olfactory bulb was obliterated; the




Central scotoma, outside of which objects and colors were clearly seen.

Slight concentric contraction; no central scotoma.

FIG. 1.—Visual fields of Case I.

left optic nerve was directly pressed upon; there was no distention of the left optic nerve sheath, whereas the lumen of that on the right side was markedly enlarged. A careful microscopic examination of the optic nerves was made by Mr. Leslie Paton, who found in the left a "compact fasciculus of degenerated fibers in the outer part of the nerve."

My second case is that of a man, aged thirty years, who was admitted in March, 1911, to the second surgical division of Bellevue Hospital, New York, under the care of Dr. John Rogers, who kindly asked me to see the case, and to whom I am indebted for permission to make use of the following notes.

A bartender by trade, he had been struck on the right fronto-parietal region by a spent revolver bullet in the course of a saloon

squabble in July, 1910. The bullet embedded itself in the bone but failed to penetrate the skull cavity; it was easily removed within a few hours of the injury, and the wounds caused by trauma and operation quickly healed. The man resumed his occupation shortly afterward. He remained in perfect health until February, 1911, when he began to complain of headache of considerable severity. He became moody and irritable and so changed in disposition that his relatives brought him to Bellevue Hospital, where he was admitted, as I have indicated, some three weeks after the appearance of symptoms. I saw him two days later, when his condition was briefly as follows: Mentally, he was clear and well orientated. A feeble jocosity of manner regarding our interest in him and the details of the examination might or might not have had pathological significance. The olfactory sense, while not lost, was definitely depressed on the right side. The pupils were normal in appearance and reactions. The right optic disk was quite clear. Its color was good, though the vessels seemed to be rather below normal in size. The left disk was completely obscured by swelling. Both veins and arteries were tortuous and congested and much exudate and many hemorrhages were visible, both on the disk surface and the adjoining retina. Visual acuity in this eye was normal. He complained of "blurring of the sight" of the right eye, but no scotoma could then be made out. Very slight facial weakness on the left side; when the eyes were closed tightly the left eyelash was always less well covered than the right. Power in the hands and arms was equal on the two sides, but there was a well-marked, rather coarse tremor in the right hand while held outstretched. Dorsiflexion of the left foot was less well performed than on the right side. The left abdominal reflexes tired before those on the right; the left knee-jerk was brisker than the right; the left plantar reflex was of indefinite character, while the right was invariably of flexor type. Sensation was normal.

The picture thus presented was that of an expanding lesion of the right frontal lobe.

The history of trauma and the rapidity of the onset of the symptoms made the theory of abscess more probable than that of tumor, but it seemed wise to have the cerebrospinal fluid examined before operating. This was done. It was disconcerting to bear that there was neither leukocytosis nor lymphocytosis in the fluid and that the Wassermann reaction in the fluid was strongly positive, a report which, coupled with another to the effect that the opthalmoscopic conditions in the left eye were the result of syphilitic neuroretinitis, seemed almost irrefragable proof that the patient was suffering not from cerebral abscess, but from general paresis. There was no history of syphilis.

The progress of events in the following ten days showed where lay the truth. Swelling and exudate increased in the left eye, the visual

acuity of which remained perfect, an impossible condition of affairs were the retinal elements themselves diseased to the degree shown by the opthalmoscope. Visual acuity rapidly sank in the right eye and a central scotoma, complete at first for colors and then for all objects, became easily demonstrable.

A few days after the presence of the scotoma became certain, a well-defined crescent of pallor became obvious on the temporal side of the otherwise normal right papilla. The sense of smell became almost completely abolished on the right side. The left hemiplegic signs became more and more evident, at first slowly, then more and more rapidly, until, on the day of operation, paralysis of the left arm and leg was almost complete.

On March 28 Dr. Rogers operated. An immense abscess was found to occupy the entire right frontal lobe; between 8 and 10 ounces of staphylococcal pus were evacuated and the cavity was drained. Recovery was exceedingly rapid. Two weeks after operation the patient was up and walking about the wards and balconies, with some increase of the deep reflexes on the left side as the sole trace of his recent hemiplegia. The central scotoma in the right visual field completely disappeared, and what is, perhaps, more remarkable, the pallor which had been observed in the temporal portion of the right optic disk gave place to the rosy pinkness of a healthy papilla.

My third case is that of an unmarried woman, aged forty-two years, who was admitted to the National Hospital, London, in March, 1909, to the service of Dr. Risien Russell, by whose courtesy I am enabled to state the following:

Toward the end of 1906 the patient began to complain of occasional dizziness and "queer feelings" in the head. In May, 1907, she had a slight generalized convulsion during sleep, which in no way incapacitated her for work (clerking) on the following day. From that date until December, 1907, when she had a second slight convulsion, she was troubled with frequent headaches, and petit mal attacks. In August, 1908, headache began to be violent, and when most severe was often accompanied by transient blindness in the right eye. Nausea then became constant and vomiting frequent. In March, 1909, vision became very rapidly dimmed, and the fundi were examined, as a result of which she was admitted to the Queen Square Hospital.

Her mental condition was apparently normal. The sense of smell was abolished on the right side, and much diminished on the left. Vision on the right side was reduced to $\frac{3}{60}$ and on the left to $\frac{3}{36}$. A central scotoma, complete for colors and objects was found in the right visual field; the left field showed a marked degree of concentric contraction, but no scotoma (Fig. 2).

*Fundi.* Left eye: Intense papilledema with numerous hemorrhages. The highest point of swelling could be seen clearly with a + 8

diopters lens, but this reading was reduced to + 6 diopters by reason of the presence of + 2 diopters of hypermetropia.

Right eye: The optic disk was very pale, with clearly cut margins. The physiological pit was seen distinctly. The vessels were below normal in size.

There was considerable weakness of both external recti muscles. Beyond slight weakness, of supranuclear type, of the left side of the face, together with increased deep reflexes on the left side, the patient did not present any further signs of localizing value.

A right-sided temporal decompression operation was performed by Mr. Donald Armour, which resulted in cessation of headache, nausea, and vomiting. Swelling disappeared from the left disk, to which eye normal visual acuity was restored. In this case

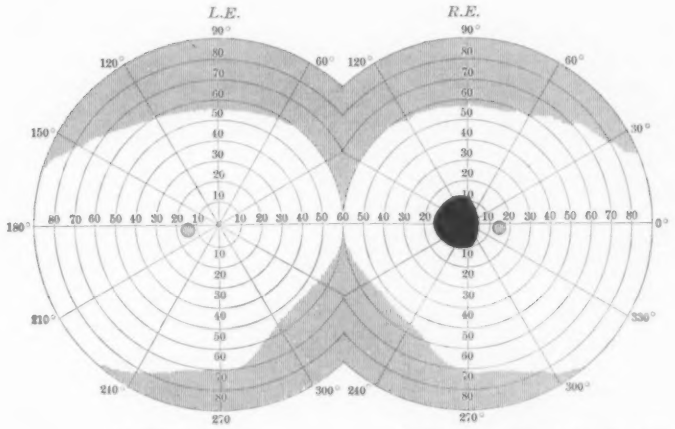



FIG. 2.—Visual fields of Case III.

however, operation had no effect on the atrophic condition of the right optic nerve. Nine months after operation the right papilla was pearly white in color and perception of light was only possible in the periphery of the right visual field, showing that the reduction of the general intracranial pressure had failed to have any effect on the local pressure exerted on the trunk of the right optic nerve.

These three cases are classed together because in each retrobulbar neuritis occurred in the nerve ipsolateral to the tumor before papilledema had had time to develop; that is, direct pressure was exerted on the nerve trunk from the very beginning of the disease. The next three cases show a somewhat different picture. Here no local pressure was exerted on the optic nerves until after the occurrence of bilateral papilledema. When local pressure eventually did occur,

the appearances due to retrobulbar neuritis were substituted for those due to papilledema.

The first case in this subdivision is that of a schoolmaster, aged thirty-seven years, who was admitted to the National Hospital in June, 1909, in the service of Dr. T. Grainger Stewart. For two years before coming under observation he had suffered from progressively severe headaches, frontal in position and paroxysmal in type. In January, 1908, he had a sudden attack of unconsciousness with general tonicity and cyanosis, followed by a considerable slurring in speech, which latter, however, passed off in a day or two. From that time he was subject to such seizures every two or three weeks; in addition, there were momentary lapses of consciousness of typical petit mal character which occurred still more frequently. Nausea was frequent, but there was never any vomiting.

In May, 1909, he began to be unsteady in walking, and considerable tremor developed in both hands. On the evening of the day on which he was admitted to the hospital he had a convulsion, which occurred during the course of my examination. He began to tremble all over, became cyanosed and slightly rigid, and lost consciousness. The corneal reflexes were abolished. The coarse tremor, which was more pronounced on the right side, continued during the two minutes of unconsciousness. After the attack there was an almost complete temporary right hemiplegia, with a passing difficulty in speech.

On examination, the patient had the appearance of one suffering from intense intracranial pressure. Attention was very defective, answers to questions were often quite irrelevant, and there was much drowsiness and frequent yawning. Patient was unable with either eye to read the largest letters on the test card. The sense of smell was markedly diminished on the left side, and was normal on the right. The right optic nerve was the seat of a steep-edged edema, the highest point of which was seen with a + 6 diopter lens. There were numerous hemorrhages on and around the papilla. The left optic disk showed a crescentic pallor in its temporal part. The physiological pit was filled in, but no swelling could be measured on the disk surface. The papillary edges were clear, but irregularly waved in outline; there was intense disturbance of choroidal pigment. Vessels were below normal in size. There was considerable weakness of supernuclear type of the right side of the face. The right arm and leg were definitely less strong than their fellows of the opposite side. The right abdominal reflexes were depressed as compared with the activity of those on the left. The knee-jerks were equal; the left plantar reflex was invariably of the normal flexor type; that on the left side was frequently not obtained, and when present was sometimes of flexor and sometimes of extensor type. There was no sensory change. The patient was frequently inconti-

nent of urine, a circumstance of which he was apparently quite careless.

On June 22 a bone defect measuring three by two and one-half inches was made by Mr. Donald Armour in the left frontal region. Intracranial pressure was extreme.

By the following day, the patient's mental condition had very greatly improved and his powers of attention had become so much better that it was possible to obtain an accurate perimetric tracing of the fields of vision. These were taken by means of an ordinary perimeter and also with a Bardsley's scotometer; the results obtained with the former failed to show any concentric or hemianopic contraction, but those obtained with the latter showed a cleanly cut central scotoma in the left visual field, complete both for colors and objects (Fig. 3).

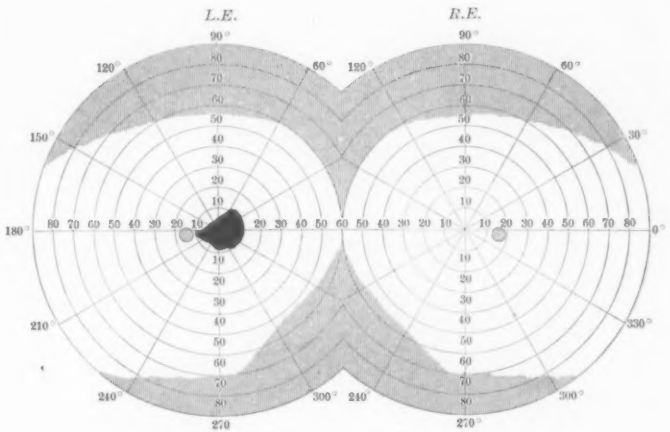



FIG. 3.—Visual fields of Case IV. Perimetric tracing taken with a Bardsley's scotometer.

The second stage of the operation was carried out after a week's interval. The left frontal lobe was completely exposed. None of its surfaces was the seat of tumor formation. A large horizontal incision was made in the lobe, which was explored with the finger. Lying deeply near the middle line there was found a thick grayish mass, which, on being opened, proved to be a cystic wall containing yellow gelatinous material. The growth was poorly defined, but apparently all of it was removed by spoon and finger.

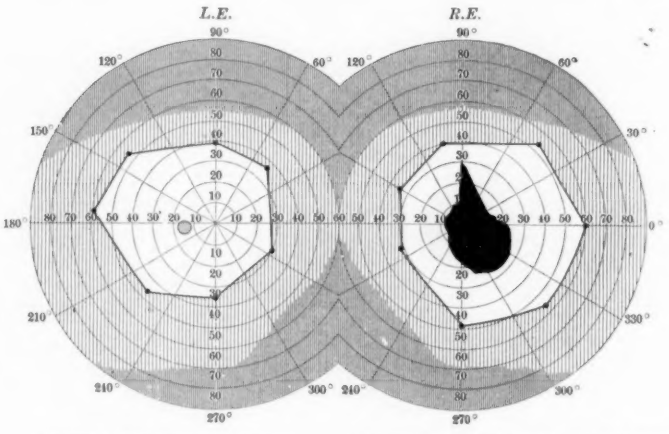
On the evening of the day of operation, the patient moved both the right arm and leg strongly, and showed no evidence of aphasia.

He made an uninterrupted recovery and left the hospital on January 3, 1909, with very slight weakness of the right limbs, the

plantar reflexes, however, being both of the flexor type. His mental condition on discharge was apparently normal.

The second case is that of a woman, aged thirty years, whom I saw in the service of Sir William Gowers, in November, 1909. She had been subject to fainting attacks since the age of seven. These seizures never possessed any of the characteristics of major epilepsy. In the summer of 1906 she began to suffer from frontal headaches, which in the next two years became very severe and were occasionally associated with transient dimness of vision, especially in the right eye.

On admission to the hospital, she stated that in August of that year (1909) she had had such a cold in the head that in ten days' time she had completely lost the power of smell in the right nostril, and vision in the right eye had so much deteriorated that she was only




Concentric contraction; no scotoma. Concentric contraction with central scotoma.

FIG. 4.—Visual fields of Case V.

able to make out the forms of large objects with that eye. This was the acuity of vision in the right eye, while that in the left had also become reduced to $\frac{2}{60}$.

A large central scotoma was found in the right visual field, together with considerable concentric contraction; the latter was also present in the left perimetric chart, but no central defect could be made out (Fig. 4). Ophthalmoscopic examination showed on the left side marked swelling of the papilla, +3 diopters in height. The color of the disk was markedly deeper than normal, and the retinal vessels were swollen and tortuous. The right papilla was edematous to an identical degree. The disk, however, was intensely white in color, and the caliber of the arteries was very markedly reduced. There was complete anosmia on the right side and considerable deterioration

of the sense of smell in the left nostril. A coarse rhythmical tremor was seen in the right hand when the hand was outstretched. The deep reflexes on the left side were increased, the left abdominal reflexes were depressed, and both plantar reflexes were of the normal flexor type. Her mental condition was distinctly abnormal; she was very excitable, laughed foolishly and causelessly; joked feebly and inappositely; was very ready to take offence, and, on the other hand, was effusively apologetic over trifles. There was no speech defect.

On November 23, 1909, Sir Victor Horsley made a large osteoplastic flap over the right frontal region, and a week later the dura mater was incised and the right frontal lobe exposed. Intracranial pressure was greatly raised. No tumor was seen on the brain surface. A vertical incision was therefore made in the right frontal lobe, which was then explored by the finger. Deeply embedded in the brain and almost resting on the orbital plate was found a hard fibrous growth, evidently of benign character, in that it was sharply delineated from the cerebral substance. It was easily removed.

Papilledema later completely disappeared, and vision improved in the left eye.

My last case is that of an elevator runner, aged twenty-six years, whom I saw in February, 1911, in Professor Dana's service at the Neurological clinic, Cornell University Medical College, New York.

Onset of symptoms dated from six weeks before his admission to the clinic, when he began to notice dimness of vision first in the left eye, and a few days afterward in the right also. For the first week he had a little dull headache over the eyes, which, however, did not trouble him greatly, and which never recurred. Deterioration of vision was progressive, and when he came under observation he was only able to see a lighted match when held in the periphery of the visual fields of either eye. With the exception of his blindness, he felt himself to be in normal health. He gave a history of having smoked upward of a hundred cigarettes a day; his consumption of alcohol had been considerable and systematic.

On examination, it was found that he was unable to smell any aromatic substance, though ammonia was at once appreciated and recognized; he had complete anosmia in both nostrils. The pupils were equal and acted briskly to light and on convergence, the contraction, however, in each case being poorly sustained.

*Ophthalmoscopic Examination.* Right eye: The optic disk edges were blurred; no venous engorgement nor tortuosity. The papillary color was about normal. No hemorrhages nor other exudate seen. The left ocular fundus showed a similar picture, with the exception of the fact that the optic disk on that side was definitely blanched, especially in its outer portion. The visual fields were as indicated above.

The right abdominal reflexes were absent, while those on the left side were obtained but once. The right cremasteric reflex was diminished. The knee-jerks were very active, the right being greater than the left. There was also an ill-sustained right-sided patellar clonus. Both of the plantar reflexes were of the flexor type.

The association of papilledema, anosmia, and pathological reflexes on the right side led to a diagnosis of left frontal tumor; he was accordingly admitted to the second medical division of Bellevue Hospital. When examined there, the unilateral reflex signs found in the Out-patient Department could not be obtained; repeated examinations over a period of two weeks failed to elicit any pyramidal signs whatsoever.

This failure to corroborate localizing phenomena, added to the retention of light perception in the peripheries of the fields, and the entire absence of all the usual signs of general intracranial pressure, such as headache, nausea, vomiting, or drowsiness, threw doubt on the original diagnosis and brought up the question of the fundal conditions being the result of either a toxic retrobulbar neuritis of tobacco and alcoholic origin, or of acute disseminated sclerosis.

The diagnosis of neoplasm was established by the patient having a severe generalized convulsion in the night of March 11; no sign indicative of the localization of the tumor was obtained until five days later, when the right abdominal reflexes were again depressed and the right plantar reflex was found to be sluggish with an occasional tendency toward the extensor type of response, while its fellow remained definitely flexor. It was accordingly decided to explore the left frontal lobe. On the afternoon of March 17 the patient suddenly had several general epileptic attacks, after which he passed into a stuporous condition, which rapidly deepened into coma. Dr. Woolsey rapidly exposed the left frontal lobe, the lower two-thirds of which was seen to be the seat of an enormous tumor, which was easily removed. The patient died before he could be brought back to bed.

The growth occupied, as has been said, the lower part of the left frontal lobe and pressed upon the sublying optic nerves, the left nerve being the one more directly involved. Microscopically, it was a glioma. It weighed 165 grams.

In this last case the tumor, by pressing on the optic nerves and olfactory bulbs of both sides, produced bilaterally a symptom complex seen in the other cases on one side only.

# A CRITICAL REVIEW OF THE SURGICAL TREATMENT OF NEPHRITIS.[1]

By Morris Booth Miller, M.D.,

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To attempt to discuss the operative treatment of Bright's disease within the limits of a short paper is somewhat difficult, in view of the extremely interesting, and at times rather animated, controversy which has enlivened the literature on this subject during the last decade. Furthermore, it must be borne in mind that we are considering a proposition over which opinions are still widely divided and wherein the evidence has not yet been marshalled in orderly array. I shall, therefore, merely sketch in broad lines the birth of the idea that nephritis may be cured by the knife, trace in more or less fragmentary manner the determination of many of the questions which have arisen, note most briefly the results of clinical and experimental observations, and, finally, offer to you certain deductions and conclusions which may be reasonably drawn at this time. To those who prefer to seek their data at their sources I may say that Edebohls' article on "Decapsulation of the Kidneys for Chronic Bright's Disease," published in the *Transactions of the Section on Surgery and Anatomy of the American Medical Association*, 1908, furnishes a long and nearly complete bibliography.

In 1896 Reginald Harrison, in the Presidential Address before the Medical Society of London, drew attention to some cases where albuminuria and other renal symptoms, thought to have been due to stone or other operable condition, had entirely recovered after nephrotomy, though no stone had been found. The operation consisted merely of incision or puncture of the kidney with subsequent drainage. He inferred from these results that the recovery was due to the restoration of the normal renal circulation through the relief of tension and congestion. He further suggested that the recognition of tension as a factor in kidney disease had not received adequate attention, and that further study along that line might lead to some revision of our views of renal pathology. Five years later he read a paper entiled "A Discussion on Renal Tension and its Treatment by Surgical Means," before the British Medical Association, in which he urged that in nephritis, the engorgement of the renal tissues was the dominant factor, and that it might properly be relieved by incision and puncture. He called attention to the well-recognized benefit arising from operation on the testicles and pancreas to relieve tension, and argued by analogy that the kidneys

[1] Read before the Philadelphia County Medical Society, March 8, 1911

were similar fibrous-covered organs and as such might be operated on in Bright's disease. Six cases were reported, in which cure or improvement had followed operation, but apparently in none of these was the operation performed for the direct cure of nephritis.

The late George M. Edebohls, of New York, stated early in 1899 that from a series of 154 nephropexies done on 118 patients, he noted in 6 there was present chronic nephritis. In the first 5 the operation was done without thought of influencing the nephritis, but inasmuch as the improvement was so striking in 3 of these 5, he decided in the sixth case to operate for that indication alone; accordingly, on January 10, 1898, the first deliberate operation for nephritis, by decapsulation, was performed. These early cases may be briefly summarized as follows: The first showed chronic diffuse nephritis, in which only one kidney was operated on, but two months later albumin and casts had disappeared. The second was also one of chronic diffuse nephritis, but no improvement followed the operation. The third had chronic interstitial nephritis of several years' standing, and in this case there was no improvement. The fourth was suffering from chronic interstitial nephritis of the left kidney, the right being healthy; in this case the urine showed no indication of nephritis four months later, and two years after operation was well. In the fifth case a right nephropexy was done on a patient suffering from chronic nephritis (type not stated), in which recovery was complete a year later. The sixth case, the one in which the operation was performed for no other purpose, a double nephropexy was done for chronic interstitial nephritis in which only the left kidney was involved. So successful was the result that a year later the patient was pronounced entirely well. Edebohls propounded the theory that the cure in these cases was based upon a new blood supply which arose from the perinephric area and attached itself to the denuded kidney, revivifying the diseased renal tissue, and gradually restoring it to a state of health. He called attention to the fact that unilateral nephritis was more common than generally thought, a point which Mr. Harrison had also affirmed.

The medical world received the announcement that this formidable disease was curable by surgical interference with the keenest interest, and at first there was a tendency to credit surgery with another brilliant victory in the domain of internal medicine. Within a very brief period, surgeons in different parts of the world commenced to record their operative results, the terms of their observations ranging from tentative approval to glowing enthusiasm. Among the more notable men who operated for the cure or improvement of chronic nephritis, were Rovsing in Denmark, Israel in Germany, Pousson, Tuffier, Talamon, and Jaboulay in France, Giordano in Italy, Ferguson, Lloyd, Gibbons, and, of course, Edebohls in America. Experimental research was undertaken to settle the questions which were raised by this novel

proposition, and valuable work was done by Claude, Balthazard, Rovighi, Johnson, Müller, Reis, Wetzel, and others. But it was not long before the opposition began to make itself felt. Led by Senator, in 1902, who was ably seconded by his fellow Germans, Rosenstein, Kümmel, Riedel, and Zondek, and in America by Conners and Porter, came a veritable avalanche of criticism, a strenuous denial of the theories which had been advanced by the two pioneers in this field, and a general refutation of the proposition that Bright's disease could in any way be influenced by surgical measures.

In order to bring into proper perspective the subject as it stands today, I shall attempt to formulate certain conclusions from the vast material now at our disposal. In the first place, it is generally agreed that albuminuria is not *per se* an evidence of Bright's disease, although the etiological factors back of it will in time, if not removed, occasion those tissue changes in the renal substance which characterize that disease. Broadly speaking, all cases of albuminuria may be divided into two classes—those in which the cause is confined to the kidney itself and those in which the responsible factor is systemic. In the first group should be mentioned, prominently, such local causes as wounds of various kinds, renal and perirenal infections, irritation arising from stone or detritus, and very particularly all those malformations and displacements which interfere with the normal circulation. In each and every form of what may be termed local nephritis the only sound method of relief must be surgical, since with mechanical causes we require mechanical measures to accomplish a cure.

A word with reference to unilateral nephritis may be of interest at this point. In many of the earlier cases which were cured only one kidney was subjected to operation. The results were explained on the theory that Bright's disease in some instances is a one-sided affair. That this is true in the strict sense that albuminuria, due to local causes, is frequently unilateral and that if it continues over a long period structural changes may occur in the affected kidney, must be admitted. But I am familiar with no postmortem findings which would tend to confirm the suggestion that systemic nephritis is ever one-sided, and there is no reasonable hypothesis why the systemic causes of albuminuria should fall upon a single kidney. To the writer, the presence of unilateral albuminuria would seem the best evidence of a local lesion, and as such would demand investigation into the status of the involved organ by operation.

The second group of cases, namely, those in which albuminuria arises from systemic causes, present far greater difficulties when it comes to studying the theoretical and practical possibilities of surgical aid. The systemic causes may be enumerated as follows: (1) Organic and inorganic poisons from without, acting through the blood; (2) overcharging of the blood with proteids; (3) micro-

organisms acting on the living cells or on the proteids in the blood, either directly or through their toxic products; and (4) putrefactive fermentation within the alimentary canal with absorption of poisonous products.

While each of these causes may occasion albuminuria for a time without ascertainable renal lesion, sooner or later, with the continuance of the cause, there come the pathological changes which characterize true Bright's disease. These changes may be chiefly found in the tubules, creating degenerative changes in the epithelial element and constituting parenchymatous nephritis; or they may affect those parts in which connective tissue substance predominates the glomerular, interglomerular, and intertubular portions, giving rise to interstitial nephritis, or finally, both the epithelial element and the connective tissue element may be involved as in diffuse nephritis. Without going into the intimate cellular pathology, it is generally appreciated that these changes are distinctly not inflammatory in type, save in the single instance of the form known as acute exudative nephritis, where there is an intense determination of highly toxic blood to the renal capillaries. It is also a part of our general knowledge that as soon as these changes have become thoroughly established they are irreparable in a strict pathological sense. Possibly this may be less absolute in the form of nephritis which affects the epithelial element, since it has been urged by some that in parenchymatous nephritis an anatomical restoration to the normal is not impossible. There is, however, no evidence to show that there is ever a retrogression of the connective tissue overgrowth in interstitial nephritis. Physiologically speaking, these changes are anything but irreparable, since the renal function possesses compensatory powers against damage second only to those of the the heart. As Porter neatly puts it, the lesions of Bright's disease can never be cured to the eye of the pathologist and histologist, but to the physiologist and clinician the cure of the disease in a physiological sense, is both possible and probable. Physiological cure comes through the remissions which characterize this disease, and these may run the gamut from transitory abatement of symptoms to prolonged absence of all phenomena covering many years. The part which wise medical treatment may play in bringing about remission need not be dwelt upon. Is there a field here for surgical aid? Surely there is nothing pointing to the possibility of the knife accomplishing an anatomical cure of Bright's disease, until the chimerical proposition of replacing diseased kidneys with sound ones is brought about. In the meantime the question remains, Can surgery bring about physiological cure?

Let us look for a moment into the various theories which have served to explain the apparent successes after nephrotomy. Edebohls claimed that recovery was due to a new blood supply coming from the perinephric structures and penetrating the denuded sub-

stance of the kidney. This proposition was thoroughly exploded by the arguments of Tuffier and Claude, working independently, as well as by others, and by the observation of Reis, who examined six hundred denuded kidneys, to find in only one slight evidence of a new blood supply. Indeed, the source of a new blood supply would remain problematical even were it possible for the kidney to receive it, since, as was pointed out by the writer in an article on perinephric abscess, read before the Academy of Surgery, the decided inadequacy of perirenal circulation constitutes a potent cause for suppuration.

Under no circumstances, then, can any weight be attached to this neovascular theory.

Harrison's idea that recovery might come through the relief of tension cannot be dismissed quite as summarily, though here again there is faulty reasoning in some particulars. In the first place, his comparison of inflammation of the pancreas and of the testicle to the kidney in Bright's disease is unfair and unsound, both anatomically and pathologically. As I have just stated, Bright's disease is not in any sense an inflammatory process, and the renal capsule is not a material factor either directly or indirectly in the morbid changes which occur beneath it. Harrison seemed of the opinion that there was actual physical stress upon the capsule, but this is extremely doubtful. Several observers have stated that in many cases it not only was not tense, but on the contrary, presented a somewhat loose and wrinkled appearance. This may not always be the case, but it is assuming much to conclude that the removal of a relatively thin connective tissue covering, which certainly can be somewhat stretched, will affect to any extent an organ of the size and character of the kidney. Furthermore, it is now well known that after decapsulation, a new capsule is formed, which is thicker and less elastic than the original one. Carried to its logical conclusion, Harrison's thought seems almost as preposterous as to assume that splitting a glove covering a tightly clinched fist will make the fist relax. In Bright's disease it is the tight fist and not the glove which is the important factor.

From another point of view, namely, that the removal of the capsule may permit of the drainage of an edematously laden, blood-engorged, and, therefore, functionless or partially functionless area, the matter of tension presents an interesting phase which shall be presently mentioned. Pel and Jaboulay evolved the ingenious theory that the cures were brought about by a reaction of the sympathetic ganglia, due to the manipulation of the kidney during operation, and Sephonger, acting on this suggestion, devised an operation by which the kidney was secured by a flap of the quadrate muscle and covered by the internal oblique so as to obtain continuous massage. There are other interesting theories on this subject, such as the renorenal reflex explanation of the cures in

bilateral Bright's, where only one kidney was operated on, but time does not permit of their discussion.

To my mind the question resolves itself somewhat as follows: (1)There is no scientific justification for the assumption that surgery, or anything else, can cure Bright's disease once it is established. (2) The majority of the theories which have been advanced to warrant surgical interference have not been convincing, to say the least. If this were all, another chapter of valiant though vain endeavor should be considered closed, but that it is not all is shown by a constantly growing mass of clinical data which is deserving of the closest scrutiny and which strongly tends to show that the physiological cure of Bright's disease through remission may be brought about by operation. Despite an immediate mortality of about 30 per cent., and a mortality of 44 per cent., within a short period, it cannot be gainsaid that the results of the operative treatment have been other than hopeful when the desperately ill condition of many of these patients is taken into consideration. The reported cases, now running into many hundreds, show a striking number of recoveries, some of which can only be described as brilliant, and it is not surprising that nearly three-fourths of the surgeons who have expressed opinions are favorably disposed and satisfied with their results. It is interesting to note in this connection that these clinical results are supported by animal experimentation, at least to the extent that such experiments can throw light upon human conditions. Rovighi found with cantharides nephritis in rabbits that all recovered after operation, while 50 per cent. of the controls died; with diphtheria toxin nephritis 50 per cent. were saved by decapsulation, while 100 per cent. of the control animals died. Claude and Balthazard drew similar deductions from experiments on dogs.

What is the secret of these undoubted recoveries? Wherein lies the merit of surgical interference in Bright's disease? Have we another empirical measure of value like unto the operation of Spencer Wells for tubercular peritonitis, and, like it, not amenable to successful analysis? I hardly think so. I believe that nephrotomy in these cases does good and often saves life because it does, and does abruptly and thoroughly, certain things which are within the mental horizon of every medical student whenever he thinks of Bright's disease. The use of cups, dry and wet, over the kidneys is one of the oldest procedures in our armamentarium; venesection, and thereby the reduction of arterial hypertension, is an oft-neglected measure of such value as scarcely to be overestimated in the treatment of the critical phases of urinary suppression. I believe that cutting down upon the kidneys accomplishes all the purposes of cupping and of bloodletting, and does it better because it tends to relieve the disturbance at its focal point. Just as in intestinal obstruction the sympathetic nerve impulses create violent peristalsis to over-

come obstruction, so we may have in anuria and uremia intense local vasomotor efforts to overcome the renal block. Furthermore, the removal of the capsule seems wise. No man can say just what part is played in the case of suppression by the edema within the kidney itself, and decapsulation certainly offers an outlet. For this reason I believe with Harrison that these cases should always be drained. There may be other explanations for the value of surgical interference in restoring renal equilibrium based upon more precise knowledge of urinary physiology, but for the present these seem sufficient.

There can be no doubt from the published reports that it is in those cases where the factors of hypertension, local and general, and of edema are the predominant phenomena that the most successful results have been obtained, while the least satisfactory subjects for the knife have been those where the kidneys were caught in the death grip of interstitial change. Particularly apt has been the operation in saving life in the severe form of Bright's disease complicating and following the acute exanthemata, of which scarlatinal nephritis may be mentioned as a type. It is in these cases, where there is a rapidly diminishing quantity of bloody urine loaded with albumin, where deafness and blindness, convulsions, and coma occur, and where dissolution seems almost certain, that some of the brilliant recoveries have been recorded. The results in chronic parenchymatous and, to a minor extent, in diffuse nephritis have been less satisfactory, but, nevertheless, a judgment based on the experience of a large number of operators would tend to make us classify the operation as worth while. The average in these forms is brought up by the distinctly good results, broadly speaking, in young people. Even where physiological recovery has not been possible the operation has often secured abatement of the more distressing symptoms and prolongation of life. Finally, those cases in which the cardiovascular changes are marked are the least favorable of all. There seems to be but little excuse for surgical interference in interstitial nephritis.

Much must depend upon the care and good judgment with which cases are selected for operation. Already enough mistakes have been made in the theory and practice of this interesting field of curative endeavor. Bright's disease is and must remain a medical entity, and it is not until medical measures have been given a fair trial and have failed that we are justified in considering surgery. When that time comes these fairly well-defined principles may be borne in mind for guidance in the individual case: (1) That operation may be hopefully done in acute nephritis; (2) that young patients are the best subjects; (3) that there is sound reason for operating for anuria or uremia, occurring in chronic nephritis; (4) that operation may be resorted to as a last desperate chance in any form of nephritis.

With respect to the operation itself, I may say that when it was first proposed and practised, the choice of an anesthetic received considerable attention for obvious reasons, but since that time the development of spinal anesthesia has placed at our disposal a measure which is singularly well suited for the more critically ill of these cases, as I can attest from personal experience. Under all aseptic precautions the kidney area is invaded through a nearly vertical incision, extending from the inferior border of the twelfth rib to a little beyond the middle of the iliac crest. The latissimus dorsi fibers are split, the erector spinæ sheath is avoided, the quadratus lumborum is incised in its length, and the deep lumbar fascia opened. The perirenal fat is quickly pushed aside by blunt dissection until the bared convexity of the kidney is exposed. The capsule is split vertically, and by a gauze-covered finger is separated from the cortex and pushed in folds well in toward the pelvis. This can readily be done without delivering the kidney. The other kidney should then be similarly treated. The wounds are quickly closed with provision for drainage by tubing. The whole procedure should be done expeditiously, and a double decapsulation should only take a few minutes.

In the successful cases it has been found that the urine shows an increase in quantity and a decrease in morbid constituents within twenty-four or forty-eight hours, and in the majority of the recoveries the physiological cure is complete in from thirty to thirty-five days.

## THE QUANTITATIVE DETERMINATION OF FUNCTIONAL RENAL SUFFICIENCY BY THE DUBOSCQ COLORIMETER; INDIGOCARMIN VERSUS PHENOLSULPHONEPHTHALEIN.[1]

A PRELIMINARY REPORT.

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(From the William Pepper Laboratory of Clinical Medicine.)

It is conceded that the most reliable individual kidney test is one dependent upon a quantitative metabolic study. By reason of the complicated conditions entailed, the requirement of particular physiologico-chemical knowledge, and the consumption of time demanded for the completion of the necessary observation, which

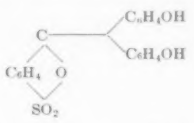
[1] Read before the College of Physicians of Philadelphia, February 1, 1911.

even then may not be conclusive as von Noorden has demonstrated, such a procedure is destined never to become popular. Indeed, the mere fact that every four or five years witnesses the announcement of a new method for determining the kidney function suffices to prove (1) that the old tests are inadequate or unsatisfactory, and (2) that it still remains the keen concern not only of the internist, but particularly of the surgeon, to find some test, whereby the health or disease of the kidney may conveniently be determined.

Various drugs and dyes have been utilized in countless attempts to solve this perplexing problem, in the subcutaneous employment of which attention has been directed to the time of onset of their elimination by the kidneys, to the constancy of reaction, and to the intensity, maximum, and duration of their excretion. Attempts to compute the quantitative elimination of these substances have never, until recently, been crowned with notable successes. Formerly, with methylene blue, in order to determine the amount of the dye excreted, the colored urine was measured and placed in a glass container. Precisely the same quantity of water was placed in another glass, and known quantities of methylene blue added until the two solutions became homogenous in coloration. The percentage of the aniline dye eliminated in the urine was then easily and approximately computed.

During the past year, Rowntree and Geraghty have called attention to the great advantages of phenolsulphonephthalein, a substance first described by Ira Remsen, for a functional renal test, placing especial emphasis upon the quantitative estimation of the percentage of the drug eliminated by the kidney during the first hour or two following its injection subcutaneously.

The structural formula of this phthalein may be represented as follows:




This substance is a bright red, crystalline powder, slightly soluble in water, but more so in alcohol; insoluble in ether; in dilute alkaline solution it is a purer red than phenolphthalein, being purple in strongly alkaline solution.

This phthalein has certain properties not possessed by phenolphthalein which recommends it highly in work on the physiology of the kidneys. It has a stronger avidity as an acid and is much more completely eliminated by the kidney than phenolphthalein. It may be administered by mouth and subcutaneously without ill effect. Employed more accurately by the latter method in doses of 6 mg. to the cubic centimeter, it is absolutely non-irritating, devoid of toxicity, and appears in the urine in normal individuals

in about ten minutes. It is also excreted in the bile, only to be reabsorbed, however, in the intestinal tract.

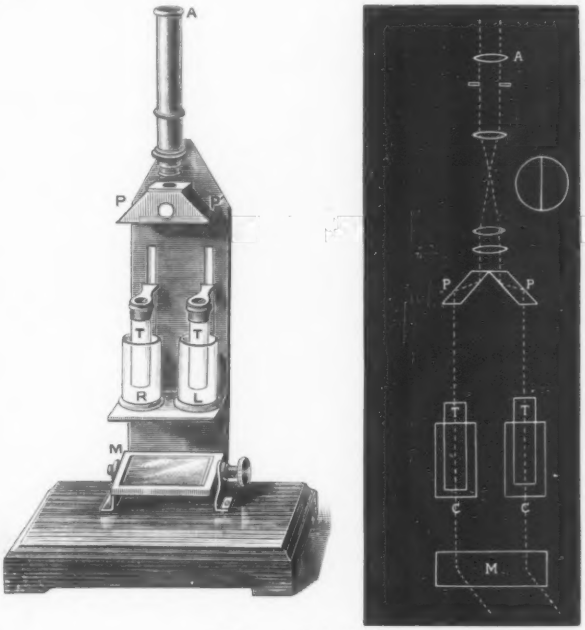
Phenolsulphonephthalein is unquestionably one of the very best substances at our command for purposes of functional renal diagnosis and prognosis. The test is very delicate, and, as is the case with phloridzin, it may prove to be oversensitive. Owing to the small quantity of the drug required for injection, which produces no pain or tenderness, it can be highly recommended to the internist for use in very sick and nervous patients, in whom it is desired to estimate the total renal function, but for unilateral diagnosis, the grave concern of the surgeon, it is extremely doubtful whether phenolsulphonephthalein can ever supplant indigocarmin.[2] The latter, although not eliminated so extensively by the kidney, has not yet been shown to be inferior to phenolsulphonephthalein as a quantitative functional test. It seems unfortunate that two such meritorious tests must be brought into comparison. It would be better, perhaps, if we were to differentiate the subjects suitable for the application of either, because in unilateral diagnosis indigo will suffice to meet the demand in cases impossible of ureteral catheterization, where the phthalein test must necessarily fail.

The technique of the phenolsulphonephthalein test is as follows: Fifteen minutes to half an hour before administering the test the patient is requested to drink two glasses of water to insure free renal activity. One c.c. containing 6 mg. of the phthalein is injected subcutaneously.[3] If it is desired simply to learn the total kidney sufficiency, as may be the case in the various forms of nephritis, or the extent of renal drainage due to vis a tergo pressure, atrophy of the parenchyma of the organs, etc., because of obstruction in the lower urinary tract, as by prostatic enlargement, etc., a catheter is introduced into the bladder and the onset of the excretion of the phthalein noted by the beautiful amethyst-red produced when it comes in contact with the drop or two of 25 per cent. sodium hydroxide placed in the bottom of the receptacle used for collection. The quantities of urine for the first and second, or possibly third, hours are then collected. Instead of the procedure by catheterization, at first continuously and then hourly, the patient may be requested to void voluntarily every five minutes until the onset is observed, and then at hourly intervals. Such a procedure is simplicity itself, but not more so than the indigocarmin technique. On the contrary, if it be desired to determine the functional activity of the individual kidneys separately, an act is demanded which may be, and not

[2] For description and technique for employment of this dye in functional kidney diagnosis, see author's articles, "Chromocystoscopy in Functional Renal Diagnosis, Based upon the Employment of Indigocarmin," Surg., Gyn., and Obstet., April, 1909, or Penna. Med. Jour., September, 1909; "Uber die Chromoureteroskopie in der funktionellen Nierendiagnostik," Zeit. f. Urologie, April, 1911; or "The Value of Chromoureteroscopy in Functional Kidney Diagnosis," Surg., Gyn., and Obstet., May, 1911.

[3] This substance is prepared by Hynson, Westcott & Co., Baltimore, Md.

infrequently is, impossible, namely, catheterization of one or both ureters, in order to convey the phthaleinized acid urine externally to an alkaline medium, so as to study the color reaction. With indigocarmin, catheterization of the ureters is rarely necessary, since the onset of the indigo elimination can be readily seen through the cystoscope as the blue jets of urine are ejected from the ureteral orifices into the bladder. Indeed, from an analysis of over one hundred cases subjected to the indigo test, the time of onset runs a close parallel to the quantity eliminated, and judging alone from the time and character of the elimination, in no instance has a false prognosis relative to renal sufficiency or insufficiency been made.




Duboscq colorimeter.

It has been alleged against indigocarmin that it does not lend itself well to colorimetric determinations. It is claimed that the urinary constituents cause a decomposition of the dye. With this statement I cannot agree, and believe that indigo is as efficient as the phthalein for colorimetric readings.

It is indisputable that for certain kidney conditions quantitative determinations are most valuable, whether the substance employed be indigocarmin, phenolsulphonephthalein or what not. During the past year or two Oppenheimer and Rowntree and Geraghty have

employed the Duboscq colorimeter with gratifying success for the estimation of renal activity, and the last two in particular are very high in their praise of the instrument.

As shown in the figures, the Duboscq colorimeter consists of two glass cylinders, cut with parallel plane surfaces placed on arms capable of vertical movement by the manipulation of set screws on the posterior surface of the instrument. These crystals may be raised and lowered in glass reservoirs containing solutions, the comparative colors of which are to be determined. In one reservoir, $R$, is placed the standardized solution; in the other, $L$, the solution to be tested. The mirror $M$ is adjusted so as to reflect light through the perforated stage, $S$, into the reservoirs supported by the same, thence to the glass parallelopipeds $P$ and $P'$, and so through the telescope to the ocular $A$. By manipulation of the set screws the crystals are elevated or lowered until a homogeneous coloration appears at the ocular. Scales, with Vernier attachments, invisible in the figures, furnish the readings from which the percentage of color in the solution to be tested can be computed.

In the performance of the colorimetric test, ½ c.c., containing 3 mg. of phenolsulphonephthalein[4] is placed in a flask and diluted up to 1000 c.c., adding one drop of 25 per cent. sodium hydroxide to elicit the amethystine coloration. This can be preserved indefinitely for future determinations. The reservoir $R$ is then about one-half filled with this control solution and the plunger lowered until the index on the scale reads 20. This reading is arbitrary, as any other may do. Within a few minutes following the subcutaneous injection of the patient with 1 c.c. or 6 mg. of the phthalein, it begins to be eliminated in the urine, occurring normally in the acid state as an orange yellow. This may be collected by voluntary urinations, by urethral catheterization, or by ureteral catheters if the work of the kidneys individually is desired. The onset of elimination is determined by collecting the urine in the presence of a drop or two of the sodium hydrate solution, noting the occurrence of the pinkish color. Quantitatively, the amounts of the first and second hours are collected separately. Each amount is rendered definitely alkaline by the addition of sodium hydrate and is diluted up to 1000 c.c. A quantity of this is filtered and placed in the reservoir $L$. The left hand set-screw is then manipulated until a similar coloration is observed on both sides, and the reading taken. If, for example, the reading on the left is found to be 40, and, as previously stated, the control reads 20, it is obvious that the solution to be tested is only half the concentration of the control, which may

[4] If indigocarmin is used, 5 c.c. of a 0.4 per cent. solution is placed in the flask for the preparation of the control solution. It will be noted that only a fractional part, in the case of the phthalein one-half and with indigo one-fourth, of the amount administered to the patient is employed in the control. This is done because the solutions in these dilutions lend themselves more favorably to colorimetric readings.

be graphically represented as follows: $\frac{20}{40} \times 100 = 50$ per cent. Inasmuch as the control is made up of but one-half in the case of phenolsulphonephthalein, and only one-quarter in the case of indigocarmin, of the amount injected into the patient, it is necessary in the former instance to divide the result by two and in the latter by four in order to determine the actual percentage eliminated of the amount injected into the patient.

The Dubosecq colorimeter is an ideal instrument for quantitative colorimetric determinations, not only by virtue of the simplicity of its construction, but also because of the accuracy of results obtained by its use. A review of Table I will demonstrate the close parallelism existing between the findings with this instrument as compared with known solutions of indigo and phthalein.

TABLE I.—Solutions in distilled water.

| No. | Known quantity of indigocarmin. | Amount estimated. | Known quantity of phenolsulphonephthalein. | Amount estimated. |
|---|---|---|---|---|
| 1 | 0.0014 gram | 0.0013 gram | 0.0027 gram | 0.0028 gram |
| 2 | 0.0039 " | 0.0039 " | 0.0023 " | 0.0024 " |
| 3 | 0.0029 " | 0.0028 " | 0.0037 " | 0.0037 " |
| 4 | 0.0056 " | 0.0057 " | 0.0042 " | 0.0043 " |
| 5 | 0.0053 " | 0.0052 " | 0.0055 " | 0.0055 " |
| 6 | 0.0071 " | 0.0071 " | 0.0074 " | 0.0074 " |
| 7 | 0.0065 " | 0.0065 " | 0.0089 " | 0.0088 " |
| 8 | 0.0087 " | 0.0086 " | 0.0087 " | 0.0087 " |
| 9 | 0.0078 " | 0.0078 " | 0.0095 " | 0.0095 " |
| 10 | 0.0093 " | 0.0094 " | 0.0098 " | 0.0098 " |

That quantitative colorimetric determinations of indigocarmin and phenolsulphonephthalein in functional kidney diagnosis are of great value is undisputed. Whether or not the quantitative estimation will in time supersede in value the onset of elimination is a mooted question and to my mind a very doubtful one, save for the determination of the total renal function particularly for the purposes of the internist. There can be little doubt that in certain conditions, as nephritis, and especially in prostatic enlargement, where, as a rule, the kidneys are more or less damaged by a vis a tergo pressure from retained urine, the colorimetric determinations are of exceptional value, and I confidently believe that every surgeon contemplating prostatectomy will not only decrease his mortality, but will also avoid debasing the profession of medicine, by refusing to operate in such cases when the total output for the first hour of indigo and phthalein falls below 10 and 20 per cent. respectively. I have long since been convinced that an onset of the elimination of indigo after twenty minutes bespeaks renal insufficiency and contraindicates operative interference. Again, it must be borne in mind that even though the quantitative elimination is found to be below the figures above stated, operation may be considered, provided the elimination during repeated determinations remains constant, evidencing no tendency to fall, thereby establishing a stable

kidney activity. On the contrary, an operation undertaken in the presence of a steadily decreasing functional capacity, as measured most accurately and satisfactorlly by colorimetric determinations, is little short of criminal, as the patient will invariably die.

An important field which should be studied, relative to the quantitative elimination of indigo or phthalein, is that of all operative cases. It is quite possible that by an analysis of several hundred cases thus tested by these substances before operation, data might be derived that would in the future lower the general surgical mortality.

The problem that I hope to solve eventually—as I do not think the results of the cases analyzed to date sufficiently conclusive—is the determination of the relative merits of indigocarmin and phenolsulphonephthalein. In order to accomplish this I have undertaken comparative studies of the action of both substances on a series of dogs and patients. It was at first attempted to study the onset of elimination of both substances from the ureteral orifices into the bladder of large female dogs by cystoscopy. The procedure was difficult, owing to the fact that the etherized dog seemed able to retain very little fluid in the bladder in the presence of the cystoscope. It was also very evident that the anesthetic (ether) markedly diminished the excretion of urine and, in one case at least, produced anuria. In the dogs subjected to indigocarmin, the fluid used for distending the bladder was water; in those injected with phenolsulphonephthalein, the fluid employed was 25 per cent. sodium hydrate. In no case was indigo or phthalein eliminated from the ureteral orifices for forty-five minutes. At the termination of that period the dogs were allowed to revive from the anesthetic. The two dogs injected with indigo immediately voided a faintly blue-colored urine; one dog having received phthalein voided at the end of an hour, the urine demonstrating the presence of that drug, the fourth dog refused to urinate. The results are tabulated below:

TABLE II.—Dogs Cystoscoped.

| No. | Substances used in tests. Indigo. | Phthalein. | Appearance of drug by cystoscopy, under ether. | Onset of secretion subsequently. |
|---|---|---|---|---|
| 1 | 20 c.c. of 0.4 % | | 0 | 45 minutes. |
| 2 | 20 c.c. of 0.4% | | 0 | 45 minutes. |
| 3 | | 1 c.c. =6 mg. | 0 | 60 minutes. |
| 4 | | 1 c.c. =6 mg. | 0 | |

Owing to the poor success of the first attempt, it was decided to perform ureterotomies under ether in the second series, catheterizing the ureters and collecting the respective urines, both for onset of elimination and quantitative study. The results are noted in Table III.

TABLE III.—Dogs Operated Upon.

| No. | Substances used in tests. | | Onset in minutes. | | Quantitive determinations. | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | First hour. | | Second hour. | | Third hour. | | |
| | Indigo. | Phthalein. | Right ureter. | Left ureter. | Right ureter. | Left ureter. | Right ureter. | Left ureter. | Right ureter. | Left ureter. | Total. |
| 1 | 40 c.c. of 0.4% | | 5 | 5 | 1.63% | 1.03% | 1.37% | 0.51% | 1.48% | 0.64% | 6.66% |
| 2 | 40 c.c. of 0.4% | | 45 | 45 | ..... | ..... | trace | 0.29% | ..... | ..... | 0.29% |
| 3 | ..... | 2 c.c. = 12 mg. | 0 | 0 | 0 | 0 | 0 | 0 | ..... | ..... | Nil |
| 4 | ..... | 2 c.c. = 12 mg. | 15 | 15 | 1.35% | 2.41% | trace | 1.32% | 0 | 0.35% | 5.43% |

Judging from the few dogs thus far utilized, there would seem to be slight preference in favor of indigocarmin. By multiplying the number of experiments with dogs, I hope eventually to throw some light on this important problem, although it is not improbable that the human subject will suffice to settle the dispute.

In Table IV are tabulated a number of cases, normal and diseased, that have been subjected to the indigocarmin and phenolsulphonephthalein tests. In a few instances, comparative applications of both methods for as many as four hours have been made.

It will be observed from a review of the tabulated cases, although too few in number for absolute conclusion, that the onset of elimination of both indigo and phthalein runs a close parallelism with the quantitative output; that as substances for quantitative determination in the estimation of renal sufficiency, they are essentially equal in value; that both substances are largely eliminated during the first two hours after injection; that the percentage output of indigo is approximately about one-half that of phthalein, which fact, however, is of no moment in drawing conclusions; that in normal ambulatory cases the onset occurs in about ten minutes, while the total output exceeds 60 per cent. of the amount injected; that in contradistinction to the ambulatory cases, the bedridden patients, even though possessing supposedly normal kidneys, excrete less than one-half of the amount eliminated by the cases at liberty to move about, and, finally, that the output of indigo occurs slightly earlier and continues no longer than the phthalein.

CONCLUSIONS. 1. Quantitative colorimetric determinations of indigocarmin and phenolsulphonephthalein are of very great value in the estimation of the total renal function, particularly in such conditions as nephritis and damaged kidneys, incident to prostatic enlargement, etc., causing poor drainage and resulting in vis a tergo pressure. These substances routinely employed by the surgeon as indicators for or against surgical intervention, particularly in contemplated prostatectomies, but likewise in other fields of surgery, will aid materially in the reduction of operative mortality.

## Table IV.—Quantitative Colorimetric Tests on Human Beings.

### Normal Cases.

| Name. | Diagnosis. | Indigocarmin. Amount injected. | Onset. R | L | Quantity eliminated. 1 hr. | 2 hrs. | 3 hrs. | 4 hrs. | Total. | Phenolsulphonephthalein. Amount injected. | Onset. R | L | Quantity eliminated. 1 hr. | 2 hrs. | 3 hrs. | 4 hrs. | Total. | Urinalysis and Remarks. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| L. S. | Normal (ambulatory) | 8 mg. | Before 10 min. | | 11.84% | 4.86% | 1.75% | 0.91% | 19.36% | 6 mg. | Before 10 min. | | 37.59% | 23.69% | 9.62% | .. | 70.9 % | Negative. |
| I. G. C. | Normal (ambulatory) | 8 mg. | Before 9 min. | | 10.86% | 8.44% | 2.06% | 1.01% | 22.37% | 6 mg. | Before 9 min. | | 58.47% | 6.28% | 3.62% | 1.4% | 69.77% | Negative. |
| S. | Normal (ambulatory) | .... | .... | | .... | .. | .. | .. | .. | 6 mg. | Before 15 min. | | 33.44% | 18.66% | 5.62% | 4.32% | 62.04% | Negative. |
| B. A. T. | Normal (ambulatory) | 8 mg. | 5 min. | | 7.53% | ? | 2.56% | 1.44% | ? | 6 mg. | Before 9 min. | | 30.12% | 18.38% | 13.58% | 3.76% | 65.84% | Negative. |

### Abnormal Cases.

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| R. C. | Nephrolithiasis (Rt.) (bedridden) | 8 mg. | 10 min. | 7 min. | 3.35% | 5.47% | 1.35% | 0.51% | 10.68% | 6 mg. | 18 min. | | 11.00% | 6.95% | 3.22% | 1.89% | 23.06% | *Urine:* negative save for few erythrocytes. Calculus 1 cm. in diameter removed. |
| W. E. | Myocarditis (bedridden) | 8 mg. | 9½ min. | 9½ min. | 10.82% | 2.07% | .. | .. | 12.89% | 6 mg. | ? | | 5.91% | 21.36% | .. | .. | 27.27% | *Urine:* Acid, 1012, faint trace of albumin, hyaline and light granular casts, cylindroids, mucus. |
| M. K. | Nephritis, interstitial, chronic (bedridden) | 8 mg. | 13 min. feeble | 0 in 30 min. | 0.90% | 0.86% | .. | .. | 1.76% | .. | .. | | .. | .. | .. | .. | .. | *Blood pressure* {Sys. =185 Dias. =125 *Urine:* Acid, 1009, cloud of albumin, hyaline and light granular casts, cylindroids, leukocytes. |
| J. S. | Nephritis; tuberculosis, pulmon. (bedridden) | 8 mg. | 9 min. | 9 min. | 4.03% | 6.49% | .. | .. | 10.52% | 6 mg. | No e | liminati | on for a | period | of two | hours. | | *Blood pressure* {Sys. =220 Dias. =125 *Urine:* Acid, 1019, cloud of albumin, many hyaline and light granular casts, few erythrocytes, mucus. |
| C. O. | Prostatic hypertrophy; cardio-renal disease (bedridden) | 8 mg. | 15 min. | 15 min. | 6.25% | 1.56% | .. | .. | 7.81% | 6 mg. | 20 min. | | 7.22% | 9.61% | .. | .. | 16.83% | *Blood pressure* {Sys. = 125 Dias. = 80 *Urine:* Acid, 1015, faint trace of albumin, few hyaline and granular casts, few red blood cells and white blood cells. |
| H. R. | Nephritis, hemorrhagic? (bedridden) | 8 mg. | 11 min. | 12½ min. | ? | ? | .. | .. | 2.04% | .... | .... | | .... | .... | .... | .... | .... | *Blood pressure* {Sys. =165 Dias. =105 *Ureteral Catheterized Specimens:* Acid, 1015, heavy cloud of albumin, leukocytes and pus cells, erythrocytes, bacteria, no casts. |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| N. A. | Diabetes mellitus (bedridden) | | | | | | | | | 6 mg. | 15 min. | 2.61% | 23.07% | trace | | 25.68% | Sugar=6.25%. |
| J. McD. | Endocarditis (bedridden) | | | | | | | | | 6 mg. | Earlier than 40, not at 20 min. | ? 3.1 % | ? 9.04% | ? 10.12% | | 13.87% 22.26% | *Urine:* Acid, 1028, large amount of albumin, pus, hyaline and granular casts, cylindroids. Lost cardiac compensation. |
| B. O. | Nephritis, parenchymatous, chronic (bedridden) | | | | | | | | | 6 mg. | 12 min. | 10.80% | 9.35% | 2.8 % | | 22.95% | *Urine:* Acid, 1021, albumin =9 pro mille (Esbach), many hyaline, light and dark granular casts, colloid casts, many white blood cells. *Blood pressure* {Sys. =140 Dias. =120 |
| D. W. | Nephritis, interstitial, chronic (bedridden) | | | | | | | | | 6 mg. | | 1.61% 2.77% | 9.34% 11.95% | 5.26% 18.56% | | 16.21% 33.28% | *Urine:* Alkaline, 1018, trace of albumin, few hyaline and granular casts, few erythrocytes. *Blood pressure* {Sys. =235 Dias. =150 |
| R. C. | Fracture, compound; amputation of leg; (bedridden) | | | | | | | | | 6 mg. | ? | 3.11% | 1.28% | 0 | | 4.39% | *Urine:* Cloud of albumin, few cylindroids, leukocytes in excess. |
| J. J. | Lymphadenectomy (bedridden) | | | | | | | | | 6 mg. | 11 min. | 22.83% | 5.18% | trace | | 28.01% | *Urine:* Acid, 1023, faint trace of albumin, hyaline and light granular casts, many cylindroids, mucus, excess of leukocytes. |
| H. S. | Tuberculosis, hip (bedridden) | | | | | | | | | 6 mg. | 59 min. | 21.36% | ? | 1.06% | | 22.42% | *Urine:* Alkaline, 1008, faint trace of albumin, few polynuclear granular casts, few cylindroids, leukocytes, erythrocytes. |
| G. P. | Varicocele, postoperative (bedridden) | | | | | | | | | 6 mg. | 30 min. | 14.04% | 10.57% | 1.01% | | 25.62% | *Urine:* Alkaline, 1022, faint trace of albumin, normal leukocytes, epithelium. |
| L. B. | Tuberculosis, os calcis. (bedridden) | | | | | | | | | 6 mg. | 20 min. | 30.03% | 1.59% | trace | | 31.62% | *Urine:* Acid, 1021, few hyaline casts, cylindroids, leukocytes in excess, mucus. |
| F. W. | Wound, gunshot, spine; monoplegia (bedridden) | | | | | | | | | 6 mg. | 12 min. | 12.72% | 1.12% | . . | | 13.84% | *Urine:* Alkaline, 1026, faint trace of albumin, mucus. |
| H. J. | Tuberculosis, spine; psoas abscesses; amyloid kidneys? (bedridden) | | | | | | | | | 6 mg. | 29 min. | trace | 0 | . . . | | trace | *Urine:* Acid, 1017, trace of albumin, hyaline, dark and light granular casts, normal leukocytes, mucus. |

2. Although each substance has its particular advantages and indications as a test, indigocarmin, at least for the purposes of the surgeon, especially in the diagnosis and prognosis of unilateral renal disease, seems just as useful and possibly more practical than the new drug phenolsulphonephthalein.

3. Phenolsulphonephthalein in many respects is an ideal substance for employment in studying the pathology and physiology of the kidney. It may possibly be more sensitive than indigocarmin, in fact, may prove to be too delicate. On the other hand, the technique of the test is extremely simple and may be employed painlessly. Preference should be extended to this drug over indigocarmin whenever it is desirable to learn the total or combined efficiency of both kidneys.

In conclusion, I desire to express my grateful appreciation to Drs. Edsall, Frazier, Riesman, and T. T. Thomas for permitting me to use material that made it possible to conduct, in part, these studies.

## ACTINOMYCOSIS IN NORWAY: STUDIES IN THE ETIOLOGY, MODES OF INFECTION, AND TREATMENT.

By Frances Harbitz,

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and

Nils B. Grondahl,

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Actinomycosis is far from being a rare disease. Cases have now been studied in nearly every country. In America, Hodenpyl[1] published studies on this disease in 1890, and 1899 Ruhräh[2] reported a large series of cases observed in America.

The first case of actinomycosis was reported in Norway as early as 1887, and since that time scattered cases have occurred, but up to this time a collective report has not been brought forth. During the last fifteen to twenty years the Institute for Pathological Anatomy has been investigating a large series of instances of actinomycosis. The material was obtained partly from autopsy and partly from pathological material sent to us by the practicing physicians in various parts of Norway.

[1] Hodenpyl, 1890, Actinomycosis of the Lungs, N. Y. Med. Record, 1890, and Erving, W., Actinomycosis Hominis in America, with Report of Six Cases. Johns Hopkins Hospital Bull., 1892.

[2] Actinomycosis in Man, Annals of Surgery, October to December, 1891.

ETIOLOGY. Our series includes 87 cases, and the lesions were distributed as follows: 45 per cent. occurred on the neck and face (all cured); 23 per cent. in the thorax (all dead); 30 per cent. in the abdomen (19 dead, 5 cured); 3 per cent. on the skin (1 dead, 1 cured).

We have reasons to believe that this represents approximately the relative frequency on various parts of the body: 56 occurred in men, 27 in women, and in 7 the sex was not given. The relative age is given: 2 occurred in the first decade (boys); 12 occurred in the second decade (10 men, 2 women); 26 occurred in the third decade (17 men, 9 women); 16 occurred in the fourth decade (10 men, 6 women); 13 occurred in the fifth decade (8 men, 5 women); 7 occurred in the sixth decade (4 men, 3 women); 3 occurred in the eighth decade (3 men).

Among the 39 cervico-facial cases, in 15 the lesions were located on the cheek especially on the maxilla, the forehead, and the parotid region; in 20 they were on the mandibular or on the submental region and in 3 they were located farther down the neck, and one tumor was on the tongue.

The infection atrium was in every instance the mucous membrane of the oral cavity, and often the part covering the gums. There was no evidence of the fungi having entered by carious teeth as is supposed to take place by Lord.

All the 39 cases recovered.

In our thoracic group the primary lesion was always in the lungs, and, as a rule, in the lower lobes. The disease simulated an atypical bronchopneumonia or pulmonary tuberculosis, with fever, dyspnea, cough, and a rusty tenacious sputum, which, as a rule, contained the characteristic sulphur granules. Everyone of these terminated fatally.

The average duration was one to one and one-half years. One lived on for eight years.

The primary lesion of the abdominal cases was some part of the alimentary tract, most often the vermiform appendix. There were no primary lesions in the rectum, bladder, or genital organs, although gravitation abscesses did extend into these organs. The disease occurred as localized abscesses most often in tne ileo-cecal region. These spread both extra- and intra-peritoneally. Liver abscesses were frequently found. The average duration of the fatal cases was one to two years.

In the two patients where the disease was primary in the skin, one had a localized abscess on the arm which soon healed. The other had a phlegmonous infection of the leg, that originated from an ulcer that started during the harvest. This man's leg was amputated, but he died.

PATHOLOGICAL ANATOMY. The lesions occur in the form of a chronic suppurative inflammation with marked infiltration and a

relatively small amount of a thick tenacious pus. The characteristic feature of actinomycotic inflammation is its advance through all tissues or organs with the development of fistulous tracts. These lead into abscesses containing the typical pus. The internal organs are attacked from the periphery, and large abscesses always result. In the later stages general infection occurs through the blood with the formation of abscesses in the lungs, liver, kidneys, etc. It does not spread through the lymphatics except near the very end of the disease. In this way actinomycosis differs from other chronic inflammations, such as tuberculosis or glanders. Microscopically nothing striking is seen. Marked hemorrhagic infiltration is often observed and the giant cells are abundant.

The striking and perhaps pathognomic thing in actinomycotic inflammation is the presence of the sulphur granules. These are formed from mycelia and often contain the so-called clubs. They vary in size, color, and consistency, and there are rather marked differences between those found in man and cattle. In man the granules are usually pin-head sized; they are round or oval; of a grayish-white or yellowish color and usually of a soft consistency; rarely are they infiltrated with calcium. The color may be green or even brownish-black. With low magnification they appear as light yellow rosettes, consisting of a central mass of mycelia which radiate toward the periphery forming radial stripes (Fig. 1). The granules are surrounded by a dense zone of leukocytes. With the high power one may at times notice club formation at the ends. If they are present, the virulence of the fungus is low. Soft small granules are always found in rapidly growing lesions. In actinomycosis bovis the granules are larger, more distinct, and have a decided yellow color. They show club formation and are often partially calcified (Figs. 2, 3, and 4). They consist then of degenerated threads having very scant power of growth on media. Spores have never been seen.

Remembering then that the characteristic things in actinomycosis are a chronic inflammation advancing through all tissues, producing fistulous tracts from which ooze a thick tenacious pus containing sulphur granules and that generalized infection occurs only through the blood stream we pass to a study of the cultural characteristics of the fungus.

Cultural Characteristics. Much work has been done by many investigators in different countries for the purpose of determining the typical growth of the pathogenic fungus or fungi, and greatly varying results have been obtained; thus Boström and a large number of others have isolated a fungus growing in aërobic cultures producing aerial hyphæ, and showing true branching; it also colors the media yellow. This type has been identified with the actinomyces occurring in nature. Then another group of workers

among which are Wolff, Israel, J. H. Wright,[3] and Shiata,[4] have isolated an anaërobic fungus from actinomycotic lesions in men. Besides these two, a number of streptothrix more or less similar to the above have been cultivated from chronic inflammations where no sulphur granules occurred.

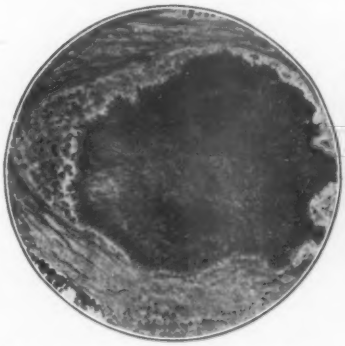

FIG. 1.—Human actinomycosis. Distinct radiation but indistinct bulbs. × 300.

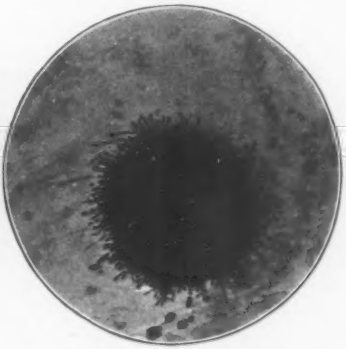

FIG. 2.—Bovine actinomycosis. Granules with marked calcification. × 300.

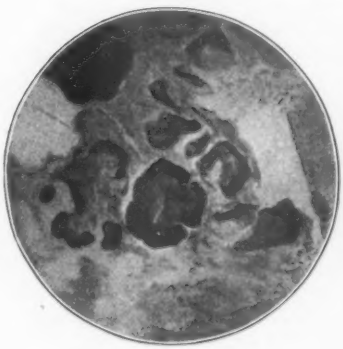

FIG. 3.—Bovine actinomycosis. × 80.

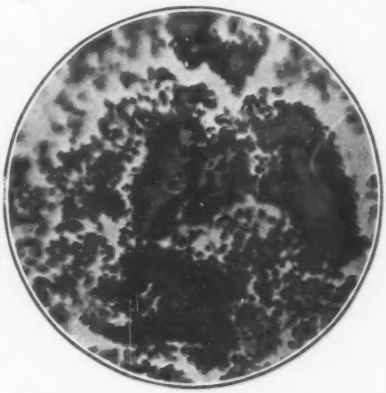

FIG. 4.—Bovine actinomycosis. Granules with marked calcification in the periphery; centre homogeneous without definite thread formation.

Because of this uncertainty as to which type was the real cause of the actinomycotic inflammation we decided to carry on a series of experiments to determine the exciting factors in our cases, and a brief statement of our work follows.

During the last year we made cultures of all the cases secured,

[3] Biology of Microörganism of Actinomycosis, Pub. of the Mass. Gen. Hosp., 1905, vol. i, No 1.
Beitrag zur Kenntniss die menschlichen Actinomycosis, Deut. Ztschr. f. Chir., 1909, Band ci.

but obtained pure cultures from only about half of them. Growth was more easily obtained from the small soft grayish granules. Pure cultures were obtained from 10 cases and seventeen strains were isolated, partly by making cultures at different times from the same lesion, and partly by inoculating media from pus, urine, or sputum from the same patient. If we add to our results the results of investigations carried on at the Pathological Institute where pure cultures were obtained from 5 cases by Dr. Kjerschow and 5 by Professor Harbitz, it makes a total of 20 cases with twenty-seven strains. Eleven of these were from the cervical facial types, three from the lungs, and four from the intestines.

METHOD. Pure cultures were obtained by putting the granules on slant agar and leaving them in daylight and at room temperature for three days. Then subcultures were made on the ordinary aërobic and anaërobic media and the cultures kept at 37° C. By this method we grew an anaërobic type, agreeing in all essentials with the one isolated by J. H. Wright. In agar stabs, the anaërobic growth was visible on the third day, and by the ninth colonies the size of a pinhead appeared as a dense zone about one centimeter from the surface. Each colony was similar in structure to a sulphur granule. Practically no growth appeared on aërobic agar slants, but it grew luxuriantly under anaërobic condition. Aerial hyphæ were never observed. In bouillon cultures grew aërobically but especially well anaërobically. Milk was not coagulated. Growth did not occur on glycerin serum, potato, gelatine, peptone broth, or raw eggs.

In order to keep the cultures alive it was necessary to transplant them about every tenth day. However, we did obtain a culture from a one hundred and forty-five day old granule. No odor, gas, or color was produced. The fungus grew very well in agar to which 1 to 2 per cent. of potassium iodide had been added. The fungus showed absolutely no tendency toward adopting an aërobic habitat, though we kept one strain through twenty generations. In old cultures the threads were branched and difficult to stain.

With the anaërobic fungus thus obtained we now carried out animal inoculations; the animals used were rabbits and guinea-pigs. Inoculations were made intraperitoneally, intrapleurally, and subcutaneously, first with sulphur granules and only once did an abscess develop in the pus of which were found granules, but this was probably not due to a real growth of the fungi. Inoculations from cultures, too, were negative. We also grew a pure culture of an anaërobic fungus, from an actinomycotic abscess in a cow, and made animal inoculations, but again failed to obtain results.

From the above we conclude that the anaërobic fungus isolated by us from many cases of actinomycosis hominis is the exciting cause of the disease in man, in at least the large majority of cases, and this conclusion is greatly strengthened by the fact that our

results are practically identical with the ones obtained by Wolff, Israel, J. H. Wright, and Shiata. It is also probable that the organism producing the disease in cattle is identical with that in man, but further work must be carried on to substantiate this.

We also examined a number of other strains supposed to be the cause of actinomycosis, but they were all aërobic and differing widely from ours. Having thus determined that the anaërobic fungus was the true cause of actinomycosis, it was left to find out, if possible, just what relation it has to the actinomyces found in nature; for botanists have obtained pure cultures and thoroughly studied many different varieties. Since we lacked time to carry on experiments to determine this relation we persuaded an able botanist, Mr. Hagen, to investigate this matter. Mr. Hagen obtained pure cultures of three strains from the air, but they were all aërobic fungi, and so were the two pure strains he secured from straw. He also grew three pure cultures from barley and oats; everyone of these had marked aërobic tendencies as had also a pure culture from manure. It might be added here that Mr. Hagen made an inoculation from an actinomycotic lesion and recovered a pure culture of the anaërobic fungus we had isolated. From his work, Mr. Hagen concluded that actinomyces hominis occurs rarely if at all in nature and if it does occur, it must exist under certain conditions only. His experiments, however, are too few from which to draw definite conclusions.

If the pathogenic fungus does not occur in nature, how, then, is the disease transmitted? Here it must be admitted that the mode of transmission is by no means clear. We have already shown that the fungus gains foothold through the lungs, the mucous membrane of the mouth or that of the intestines, but whence does it come? Is it found in the organism or on the outside and through what medium does it enter tissues? These are questions yet to be solved.

Up to this time it has been taken for granted that the fungus producing the disease in men is identical with the exciting cause of actinomycosis bovis. This has not been definitely proved. Actinomycosis hominis has also been thought to occur more frequently among country people associated with cattle. This we have found not to be the case. It is as common in cities as among farmers. Infection to man from cattle is, therefore, not probable, and since the disease always occurs as isolated cases in far separated localities, we are not justified in assuming that direct infection from man to man occurs.

It has been supposed that the pathogenic fungi are carried to the tissues by straw, slivers, and other parts of plants. This hypothesis has been based on two things: (1) That the natural and the pathogenic fungi are identical. This we have shown to be erroneous. (2) That straws, slivers, etc., have often been found in actinomycotic

abscesses. Pieces of plants are found especially frequently in the mouth lesions of cattle (Fig. 5). One must bear in mind, however,

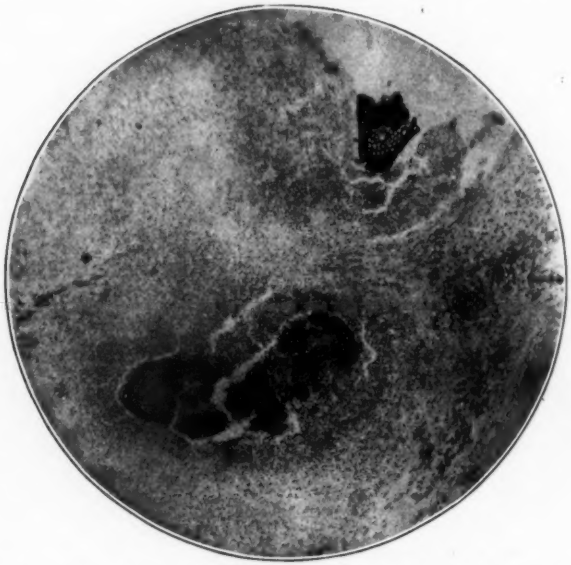

FIG. 5.—Actinomycelial granule lying beside an awn in actinomycotic bovine granulation tissue. × 80.

FIG. 6.—Cross-section of awn with actinomycosis in the central canal and growing outward. From bovine tongue. × 300.

that these might have entered the abscesses secondarily. But straws have also been found in cervico-facial abscesses in man. To be sure, such findings are much rarer in man than in cattle, never-

theless, pieces of plants do occur. It is of special interest to note that abscesses always developed after a latent period varying from months to years after the entrance of such *corpora aliena*. Abscesses have also occurred after puncture of the mucous membrane with wooden splints, fishbones, pieces of glass and in one of our patients, after an abrasion on the leg. The finding of mycelial threads in or around these objects has served to strengthen the idea that they are the real carriers of the infection (Fig. 6). There is then some definite evidence showing that straws, splinters, etc., do play an indirect role in the transmission of actinomycosis, but there is certainly nothing to prove that the disease is directly transmitted by them.

Since the fungus is not carried directly from the outer world into the animal tissues the idea that it lives as a saprophyte on the mucous membrane and enters the tissue to produce lesions naturally suggested itself. It must also be remembered that infection does not take place by the granules, since they are a pathological product produced after the fungus has gained foothold. Infection then must occur either through threads or by some unknown form. Two possibilities confront us—(1) either the fungus lives as a saprophyte on plants to enter man by chance and then to go on living a saprophytic existence until a *locus minoris resistentiæ* is offered, when it becomes at once pathogenic, or (2), as J. H. Wright has suggested, the fungus is pathogenic from the start and lives on the mucous membrane ready to enter the tissues when aided by foreign bodies. Where the fungus might originate, Wright does not suggest. Both the above hypotheses depend on the demonstration of the fungus on the mucous membrane. What is known concerning this?

Mycelia, thought to be actinomycotic, have been found by Miodowski in the tonsils and the ductus lacrimalis. But much weight can not be placed on these findings since cultures were never made.

But we obtained from the tear sac of a student who had been suffering for over a year from a chronic dacryocystitis, a granule consisting of mycelia, and closely simulating the sulphur granules of actinomycosis. From this granule inoculations were made and a pure culture of an anaërobic fungus was grown. The cultural characteristics of this strain were very much like the ones of the fungus grown from actinomycotic lesions. Whether this fungus was the cause of the dacryocystitis or not is hard to determine, but the finding of it does indicate that the fungi may be present on the mucous membrane.

Finally, a word about the existence of actinomyces in carious teeth. Professor Partsch[5] and his pupils have reported the findings

[5] Jaehn, Die Acktinomycosis des Mundes. Deut. Monatschr. f. Zahnheilk., Heft 1 to 3. 1909.

of numerous sulphur granules in decayed teeth and in the pus of perialveolar abscesses. These again simulated those producing actinomycosis only morphologically. No cultures were made. J. H. Wright and Lord[6] carried on some very interesting experiments along this line. They obtained from carious teeth mycelial threads like those of the pathogenic fungus. These they inoculated into guinea-pigs and observed the formation of abscesses containing typical sulphur granules. Unfortunately they did not recover the fungus in pure cultures. We also inoculated material from carious teeth taken both from people who were well and from patients suffering from actinomycosis, but our results were invariably negative.

It is plain from the above that nothing very definite is known about the habitat of the actinomyces hominis prior to its attack on the tissues. Further investigations along this line are called for.

TREATMENT. In conclusion, a few words about the treatment of this disease. Up to the present time it has consisted of local surgical treatment and internal medication. Locally the lesions is removed entirely when practicable, but this can seldom be done, hence surgeons often resort to curettage or simple incision. Local injections of potassium iodide have been tried. Potassium iodide has also been given internally and good results claimed. But since we have shown that the fungus grows luxuriantly in 1 to 2 per cent. potassium iodide, its curative value is doubtful. The behavior of the disease is so extremely varied that the effect of any treatment is hard to judge.

The fact that a great variety of medicines have been recommended in the treatment of actinomycosis plainly shows the need of a specific treatment. But, in order to obtain any kind of serum therapy, great obstacles must be overcome: (1) The organism is hard to grow, their pathogenicity for lower animals is slight, to say the least. (2) The production of toxins is scant. (3) It is next to impossible to use the mycelia in agglutination tests.

French investigators have developed a serum which will coagulate spores of streptothrix. This serum is secured from various mycotic diseases, including blastomycosis, but this, even at its best, can only be used in differentiating mycotic diseases from those of bacterial origin. We tried their methods, but obtained only negative results. We also tried the fixation of the complement according to Wassermann's technique, but the results were not satisfactory. Hence we conclude that agglutination tests and fixation of the complement are of no clinical value in the diagnosis of actinomycosis.

Since practically no work has been done so far on a specific vaccine,[7] we undertook to see what could be done in this line. Our

[6] A Contribution to the Etiology of Actinomycosis, Boston Med. and Surg. Jour., July 21, 1910.

[7] J. H. Wright has told us personally he has tried two cases, Dr. Jensen has used it, and Wynn reported a case successfully treated with a sort of a vaccine.

method was briefly as follows: It is impossible to count the microbes; we took, therefore, three pea-sized bouillon cultures, ground them up in 5 c.c. of normal salt solution and put them in a shaker for twenty-four hours. The mixture was then drawn up into long glass tubes, heated to 80° for three hours, and using this as a stock mixture we made two solutions from it: (*a*) 1 c.c. of the mixture plus 50 c.c. of 0.9 per cent. NaCl plus 2 drops of lysol: (*b*) 4 c.c. of the mixture plus 50 c.c. of 0.9 per cent. NaCl plus 2 drops of lysol. From solution *a*, $\frac{1}{4}$ to 1 c.c. was injected subcutaneously every second and third day, later solution *b* was tried, using 1 c.c. every second day. We never observed any local reaction from these injections. With this vaccine two patients suffering from a severe infection were treated, with the following results.

The first patient was a boy suffering from abdominal actinomycosis and with several large abscesses in the liver. He received five doses of solution *a* at intervals of from two to four days. The injections had apparently no effect, and the case went on to a fatal termination. The second, a man, aged twenty-two years, also suffered from the abdominal type. He had several large abscesses and one had penetrated the bladder. For three months this man received every second day an injection, in the beginning of solution *a* and later of solution *b*. At first he seemed to improve but soon his fever increased, dyspnea appeared and with it cough and pain in the epigastrium. After a few weeks, however, he began to improve and from then on the improvement was steady and marked. Today he is working and is practically cured, but there yet remains a soft swelling on the left side.

We have then one good result, but of course, no great weight as to the value of the treatment can be placed on it. Further trials with a specific therapy are certainly justifiable.

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## CONCERNING THE PRESENCE OF THE EMBRYOS OF TRICHINELLA SPIRALIS IN THE BLOOD OF PATIENTS SUFFERING FROM TRICHINIASIS.

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It is now two years since Herrick and Janeway[1] first demonstrated the embryos of Trichinella spiralis in the blood of a patient suffering

[1] Demonstration of the Trichinella Spiralis in the Circulating Blood in Man, Archives of Int. Med., 1909, iii, 203.

from trichiniasis. This most interesting and important finding came as a logical sequence of Staübli's[2] previous experimental work on the mode of dissemination of the embryos in guinea-pigs.

And yet, in spite of the time which has elapsed since this discovery was announced, I have been able to find the reports of but four additional cases.

During the past winter at the Presbyterian Hospital, New York, 4 cases were investigated with special reference to this point. In 2 of these the embryos were found in the blood. In the other 2 several specimens of blood were thoroughly searched, with negative results. Of the negative cases, one was proved to be trichiniasis by the demonstration of the parasites in the muscle, while the diagnosis in the other was never definitely settled.

Trichiniasis is a disease in which the diagnosis may often be made with a fair degree of certainty by the history, physical signs, clinical course, and the eosinophilia, without recourse to the examination of the blood or muscle for parasites. In these well-marked cases there is, perhaps, no great urgency for the use of further means of settling the diagnosis, except in so far as every case is more satisfactory when worked out to the limits of its possibilities.

There are, however, many cases in which the diagnosis is by no means so clear, and in which every means at our disposal must be employed to settle the nature of the disease. Two cases of those reported in this article illustrate this point.

In one, the patient was admitted to the hospital with a diagnosis of typhoid fever. A blood culture being sterile, a Widal negative, and the temperature falling to normal in the course of three days, this diagnosis was abandoned and the case was being considered one of influenza, when an embryo of Trichinella spiralis was recovered from the blood. Subsequent to this the eosinophiles, which had previously not exceeded 5 per cent., rose to 14 per cent.

The other case was even more interesting, although the diagnosis was, unfortunately, never settled definitely. The patient, a woman, was admitted to the hospital with an eighteen-day history of gastro-intestinal symptoms and fever, followed by urticaria and purpura. When admitted, the eruption was marked, but she had no fever. The leukocytes varied between 25,000 and 43,000, and the eosinophiles between 0.3 per cent. and 75 per cent. Her husband was later admitted to the hospital, having been taken ill eighteen days after his wife. A piece of muscle removed from his calf showed many trichinellæ. All possible means of settling the diagnosis in the woman were resorted to. A blood culture was sterile, no ova or parasites were found in the stools, examination of

[2] Klinische u. exper. Untersuchungen über Trichinosis, Verhandl. des Kongress f. klin. Med. Wiesbaden, 1905, p. 354; Beitrag zum Nachweis von Parasiten im Blut, Münch. med. Woch., 1908, lv, 2601; Trichinosis, Wiesbaden, 1909, Verlag von J. F. Bergmann.

the blood for embryos was negative, and a piece of excised muscle showed only "interstitial myositis," similar to that produced by trichinellæ. From the history of the case, the leukocytosis and marked eosinophilia, the muscle findings, and the fact that her husband was suffering from trichiniasis at about the same time, it seems not improbable that the patient was a victim of that disease. The case is interesting from its relation to that little understood group of cases known as "idiopathic purpura." The future examination of the blood for parasites in cases similar to the above may show that in a few the underlying condition is trichiniasis.

Method of Examination. Staübli's[3] original method of diluting the blood with ten volumes of 3 per cent. acetic acid was used, the only modification being that, in several instances, the blood was obtained from the blood cultures taken on the patients. These cultures were the usual routine ones, used in the hospital, 10 c.c. of blood being divided between two Erlenmeyer flasks of meat infusion broth. After the culture had been reported sterile, the clear supernatant broth was decanted and ten volumes of 3 per cent. acetic acid were added to the sediment. The mixture was thoroughly shaken, centrifuged, and the supernatant fluid poured off. If the resulting sediment was too thick, the laking with the acid was continued until a sediment was obtained in which the search was unhampered by the presence of countless numbers of blood cells. A drop of the sediment was then poured on a large slide, covered with a good-sized cover slip, and systematically searched with a low-power lens.

The embryos appear as a distinct, cylindrical, generally slightly curved little worms, with a refractile outline and a characteristic granular internal structure. Both ends are somewhat rounded. The anterior end is a little narrower than the rest of the body, and ends in a little, clear, homogeneous cap. The obliquely placed clear band, mentioned by Staübli,[4] as forming a line of demarcation between the anterior quarter and posterior three-quarters of the body, was not observed in the embryos studied. According to him, this band is especially well seen in the stained preparations (see illustration). Foreign substances in the sediment, such as cotton fibers, thin plugs of red cells, and fungus growths, may at first cause some confusion, but when once seen, the embryos are quite characteristic.

The embryos found in the present cases measured from 0.005 to 0.007 mm. in breadth and from 0.1225 to 0.1295 mm. in length.

By rimming the cover slip with vaseline or cement, the preparation may be preserved for several weeks.

[3] Verhandl. des Kongress f. klin. Med. Wiesbaden, 1905, p. 354; Münch. med. Woch., 1908, lv, 2601.

[4] Trichinosis, Wiesbaden, 1909, Verlag von J. F. Bergmann.

Numerous smears of the sediment were stained by various methods, but none of the parasites could be found. Herrick and Janeway had a similar experience. Staübli, however, had no difficulty in obtaining stained specimens which show the clear band at the anterior part of the parasite very distinctly.

None of the parasites was found in the stools.

The following is a brief review of the cases examined. They were all admitted to the Second Medical Division, and I am indebted to Drs. James Kinnicutt and Bovaird for permission to use the clinical facts here given.

FIG. 1.—Embryo of trichinella spiralis in blood sediment from Case II. The microphotograph was taken by Dr. Hugh Auchincloss, New York.

CASE I.—A woman, aged twenty-nine years, was admitted to the hospital on December 21, 1910. Eighteen days before admission, while working in the house, she was taken suddenly ill with pain in the upper part of her abdomen. This pain was severe, gnawing, continuous, and without radiation. At times her whole abdomen was tender. She had severe diarrhea, ten to twelve movements a day, the stools being foul and watery, but containing no blood. With the onset of pain, she complained of headache. She suffered from these symptoms much of the time for nine days, when she entered the Norwegian Hospital, where it was at first thought that she was suffering from typhoid fever. During the week that she remained there she suffered from soreness and stiffness of the left side of her

neck. There were two epistaxes. All of her symptoms cleared up and she left the hospital feeling well. Three days before admission to the Presbyterian Hospital, after drinking a glass of wine, the pain in her abdomen returned. It was relieved by vomiting and did not again appear. Two mornings before admission she noticed itching of her legs, and found them covered with large, raised, white blotches. The next day the eruption appeared about her waist, and on the morning of admission on her arms.

PHYSICAL EXAMINATION. Old herpes on lip. No puffiness of the face. Spleen not palpable. There is a remarkable purpuric, and in places ecchymotic, rash covering a large part of her body. The face, thorax, and upper part of the abdomen are not involved.

There was at no time any muscular tenderness. She had no fever. The rash gradually faded in the course of a week, but not without the appearance of fresh spots. She left the hospital on January 17, in good condition.

Seven blood counts showed a leukocytosis varying between 25,000 and 43,000, and an eosinophilia between 0.3 per cent. and 75 per cent. On several examinations no ova or parasites were found in the stools. A blood culture taken on admission was sterile and no parasites were found in the blood sediment from this culture.

Three days after admission 10 c.c. of blood were drawn from an arm vein and examined for parasites, but with negative results.

Three weeks after admission a piece of muscle was excised and examined. The pathologist returned the following report: "Between the muscle bundles is a slight increase in the fibrous tissue in spots and deposits of small numbers of lymphoid cells. The changes are similar to those produced by trichinæ. No trichinæ found. Diagnosis, interstitial myositis, probably due to trichinæ."

CASE II.—A man, aged twenty-nine years, was admitted to the hospital December 29, 1910, with a history of malaise and chilliness for nine days. Four days before admission he went to bed with these symptoms, plus general muscle pains and swelling of the face and hands. He had no gastro-intestinal symptoms at any time. His brother was taken ill at the same time, and it was found that they had both eaten pork of their own cooking shortly before the onset of their illness. The brother entered a hospital in Pennsylvania, and it was impossible to obtain a specimen of blood for examination.

Physical examination showed nothing abnormal except a fine, punctate rash over the abdomen, thorax, and arms.

For three days he had a temperature in the neighborhood of 103°, gradually falling to normal.

The blood count showed 10,000 leukocytes and 11.5 per cent. of eosinophiles. A blood culture taken on admission was sterile. From this culture four embryos were found.

The patient refused permission to excise a piece of muscle.

CASE III.—A man, aged thirty-four years, the husband of Case I, was admitted to the hospital on December 31, 1910, with a ten days' history of malaise, chilliness, and indefinite pains in the back of his neck and in his limbs. At times he noticed puffiness of his eyes. He had eaten pork three weeks before admission.

*Physical Examination.*—There is no puffiness of the face. He holds his head well turned to the right. Rotation causes pain in the posterior neck muscles, which are, however, not tender to pressure.

He had a temperature of 104°, gradually falling to normal in the course of three days.

His leukocytes varied from 15,000 to 23,000, and his eosinophiles from 2 per cent. to 41.3 per cent. The blood culture taken on admission was sterile. An examination of all the sediment from this culture was fruitless.

On January 5 a piece of muscle was removed from the calf. It was found to contain many embryos.

Following this finding another search of the blood was made on January 9. Ten c.c. of blood were drawn from an arm vein directly into 3 per cent. acetic acid. No embryos were found in the sediment.

CASE IV.—An Italian, aged twenty years, was admitted to the hospital on January 5, 1911, complaining of backache and general malaise for five days and indefinite pains in the bones, joints, and back for three days. At times he had rather mild colicky pains in his abdomen. Had some fever.

Physical examination showed slight puffiness of the eyelids and cheeks, a coated tongue, palpable spleen, and a few fine, reddish, punctate spots over the abdomen and chest. There was no muscular tenderness.

His temperature on admission was 104.4°, gradually falling to normal in the course of a few days.

Three blood counts were taken, as follows: January 5, leukocytes, 12,000; eosinophiles, 3 per cent. January 7, leukocytes, 12,400; eosinophiles, 5 per cent. January 12, leukocytes, 15,600; eosinophiles, 14 per cent.

A blood culture taken on admission was sterile. From this one embryo was recovered:

The patient would not consent to the removal of a piece of muscle.

There follows a list of the cases so far reported, together with those of the present series:

1. Herrick and Janeway.[5] April, 1909. They investigated 8 cases in one family. In 4 the blood was examined, but in 1 only were the embryos found. In that case they were found on two different occasions, on the tenth and twelfth days after the onset.

[5] Loc cit.

2. Packard.[6] April, 1910. The embryos were found in the blood twenty-two days after the onset. They were recovered from the muscle "a few days" later.

3. Barach and Mercur.[7] May, 1910. The parasites were found in the blood fourteen days after admission. The time of onset was not given. Sixteen days after the parasites had been found in the blood they were recovered from the muscle.

4. Cross.[8] September, 1910. Three embryos found on the eighth day after the onset. In this case only 1 c.c. of blood was taken. It was drawn from the lobe of the ear. Cross suggests that "it may be easier to obtain the parasites from the mixed arterial and venous blood than in the blood which has traversed the capillaries and is taken from the vein."

The patient would not consent to the removal of a piece of muscle.

*Cases of the Present Series.* 1. No embryos found on the nineteenth and twenty-second days after the onset. Six weeks after the onset a piece of muscle showed only "interstitial myositis."

2. Embryos found on the ninth day after onset. Muscle not examined.

3. Search for embryos negative on the thirteenth and nineteenth days after onset. Found in the muscle fifteen days after onset.

4. Embryos found on the sixth day after onset. Muscle not examined.

From the above it will be seen that the earliest time at which the embryos were found was on the sixth day after onset, and the latest twenty-two days after the beginning of the disease. In these cases the time of onset has been taken as the only available fixed date. It has many disadvantages over Staübli's method of reckoning from the time of eating the trichinellous meat. But he was dealing with animals where the date could be easily ascertained, whereas with human beings it is very difficult to find out at what time they have eaten infected material. Indeed, it is often impossible to obtain a history of having eaten such material at all.

Staübli,[9] from his experiments with guinea-pigs, concludes that the birth of the embryos begins, at the earliest, six or seven days after infection, and that the maximum migration in the blood lies between the eighth and twenty-fifth days after eating the infected meat. He was unable to find embryos in the heart blood of guinea-pigs later than the twenty-seventh day after infection.

The variation in the incubation period of the disease is so great that it is impossible to accurately correlate the figures given above

[6] Trichinella Spiralis in Human Blood, Jour. Amer. Med. Assoc., 1910, ii, 54, p. 1297.

[7] A case of Trichinosis with Recovery of Parasite from the Blood and Muscle, Archives of Int. Med., 1910, v, 530.

[8] A Case of Trichinosis; Trichinella Found in Blood Taken from an Ordinary Ear Puncture Archives of Int. Med., 1910, vi, 301.

[9] Trichinosis, Wiesbaden, 1909, Verlag von J. F. Bergmann.

with those of Staübli. However, in general, it may be said that the time of maximum migration agrees fairly well in the two sets of cases.

Braun[10] is authority for the statement that the adult parasites continue to live and give off embryos for from five to seven weeks. This would certainly indicate that it may be possible to find the embryos in the blood at a later date than those given above.

There seems to be an impression that it is useless to search for the parasites in the blood after they have been found in the muscle. While no cases have been cited to prove the contrary, Packard found them in the blood only "a few days" before their recovery from the muscle. The first embryos reach the muscle on about the ninth or tenth day after infection, leaving a period of from two to three weeks when there is still a fair chance of recovering them from the blood.

Conclusions. 1. In the examination of the blood sediment for the embryos of Trichinella spiralis we have a valuable means of diagnosis in cases suggesting trichiniasis.

2. From the meagre number of cases so far reported, it would appear that the method had not been used as frequently as its value would merit. It must be remembered, however, that even under favorable conditions, this method is not infrequently unsuccessful.

3. The technique of the examination is very simple. While the search for the embryos is tedious, it is scarcely more so than the examination of the blood for the plasmodium of malaria.

4. The earliest time at which the embryos may be found in the blood is on the sixth or seventh day after infection. The latest date is not so accurately fixed. While the parasites have not been found later than the twenty-seventh day after infection in guinea-pigs, or later than the twenty-second day after the onset of symptoms in man, there is some ground for the belief that they may occasionally be recovered in the fifth or possibly the sixth week after infection.

5. This method is of greatest value in those cases where the diagnosis is doubtful and especially where the patient refuses permission to excise a piece of muscle or where the muscle findings are negative.

[10] Die Tierischen Parasiten des Menschen, Wurzburg, Verlag von A. Stuber, 1908.

# BACTERIN TREATMENT OF SEPTIC RHINITIS OF SCARLET FEVER, WITH REPORT OF ONE HUNDRED CASES.[1]

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Since the exact cause of scarlet fever is unknown, the problem of infection and the illness of the "return case" is very perplexing. Until comparatively recent times the desquamated epithelium was regarded as the chief infectious agent. Gradually the infectious character of discharges from the upper air passages and especially the nose is being recognized. However, until the exact contagium is discovered to explain some of the paradoxes of infection in scarlet fever, the question of infection will always be in doubt. While many of those having considerable experience with the hospital management of scarlet fever may be dubious of the infectiousness of the epithelium of late desquamation, everyone recognizes the danger lurking in discharges from the upper air passages.

In this connection, the report on "return cases "of the Metropolitan Asylums Board[2] of London is of much interest. This report shows that, of 1361 patients discharged from the hospital with some evidence of desquamation, only 94 cases, or 14.5 per cent., were associated with the illness of "return cases," and in the majority of these "infecting cases" another morbid condition co-existed which was sufficient in most instances to account for the illness of the "return case." For instance, in 60 cases a morbid condition of the nose or postnasal region existed. In only 24 cases was desquamation alone present. On the other hand, there were 125 "infecting cases," equivalent to 19.2 per cent., in which apparently no morbid condition, as desquamation or nasal discharges, was present. So that, whatever may be said of the early desquamation, the evidence adduced would seem to show that the late desquamation is not infectious. The same report shows that in 52 per cent. of cases a morbid condition of the nose was the lesion associated with the illness of a "return case." This percentage agrees closely with the records of the Philadelphia Hospital for Contagious Diseases, and emphasizes the important relation between the nasal discharges of convalescents and the spread of scarlet fever.

[1] Read by invitation before the Philadelphia County Medical Society, April 12, 1911.

[2] Metropolitan Asylums Board. A Report of Return Cases of Scarlet Fever and Diphtheria, Henry Kemmshead, London, 1902, p. 19.

Nasal discharge in scarlet fever patients are usually very persistent and refractory to treatment. While bacterin therapy has been used with success in both acute and chronic rhinitis of non-scarlatinal origin we have not been able to find any reference to its use in the treatment of the rhinitis of scarlet fever. This report is based upon the bacterin treatment of one hundred such cases of septic rhinitis, treated in the scarlet fever wards of the Philadelphia Hospital for Contagious Diseases.

Many patients have discharging noses early in the disease when admitted to the hospital, others develop the condition shortly after admission, but in the large majority of cases this purulent or non-purulent rhinitis develops during convalescence, frequently just preceding dismissal from the hospital. The nose is always most carefully examined by Dr. Woody, chief resident physician, three different times before the patient is permitted to go home, and if only suspicious of discharge the patient is detained in the hospital. In this way the period of residence in the hospital is frequently much prolonged.

It is a difficult matter to adopt a good working classification of these nasal conditions. We have divided them for convenience into purulent and non-purulent rhinitis. The former is characterized by a profuse mucopurulent discharge which produces considerable excoriation about the nostrils and upper lip. The lower turbinates are congested and edematous and covered with this glairy purulent material. Crusts form about the nostrils, and the child invariably picks at these, soon producing a swollen, bleeding, crusty, painful condition. Children under four years of age cannot cleanse their noses by blowing, and irrigation is dangerous and often impossible. Splinting the elbows or tying the hands in mittens to prevent picking, with simple cleansing and the application of protective and soothing ointments, is about all one may do. The course of the disease in the majority of these cases is frequently prolonged and most tedious. Less severe cases show swelling of the turbinates with a small fissure at the mucocutaneous junction, with a thin, watery, scalding discharge.

In the non-purulent cases the turbinates are enlarged and the discharge is profuse, thin, and watery, or mucoid, and irritates the nostrils and upper lip. In the mildest cases there is present a moisture about the anterior nares, with redness and tenderness of the nose. We endeavored to separate ordinary acute colds, in which the discharge is purely mucous, from the rhinitis under discussion, in which the discharge is more apt to be serous or seropurulent, septic, and very irritating in character.

We believe that this rhinitis is, in itself, specifically infectious. Kerr[3] states that "it is undoubtedly infectious from patient to

[3]Text-book of Infectious Diseases, Oxford Med. Press, first edition, 1909.

patient and plays a prominent part in the production of the return case." We have noted, on two different occasions, an outbreak of this rhinitis in a convalescent ward of patients with healthy noses, to follow in from two to four days the introduction of a rhinitis case from another ward. Adenoids especially predispose, and these complicated cases resist all treatment. The younger and weaker patients are quite prone to suffer with this septic rhinitis. The warm bath preceding dismissal from the hospital has been a fruitful source by lowering both general and local resistance. Since this has been eliminated by giving the disinfecting bath on the day previous to discharge, fewer cases develop rhinitis prior to discharge or upon reaching their homes.

What part does nasal discharge play in the etiology of "return cases" of scarlet fever? Some persons believe that these discharges are not infectious *per se*, but rather that the scarlet fever infection is derived from acute cases and engrafted on the patient. Simpson[4] points out "that the infection, the causal microörganisms, appears to acquire activity particularly in the mucous discharges, whether acute or chronic, but further than acting as suitable media for their growth and carriers of any possible infection that may come in contact with them the discharges do not appear to possess infectious properties of themselves."

If the secretion dries up, there is no longer the medium on which the microörganisms can engraft themselves, so that the patient becomes non-infectious.

Others believe that the "infecting case" at the time of dismissal has not entirely eliminated the infection derived from the original attack, and as a consequence the discharges remain infectious. This view is hardly tenable. We are led to agree with the views of Cameron,[5] who believes that the causal microörganisms of scarlet fever lead a saphrophytic existence in the mucous membranes, and when conditions are favorable retain their vitality for a considerable period of time. In most cases the conditions are unfavorable and the infection dies out, but in other cases it may live and retain its vitality, especially upon a mucous membrane impaired either by a general lack of vigor or by a superadded local, septic infection. For this reason an "infecting case" may be one of poor vitality without a local lesion in the nose, and this agrees with the clinical observation that a discharge is not necessary to the patient's infectiousness. This superadded septic infection may be acquired either before or after admission to the hospital by extension of infection from the throat, inhalation of dust, etc. A warm bath followed by chilling of the body may so lower vital resistance as to favor activity of septic organisms in the mucous membranes.

We began the bacterin treatment of these cases with the hope of

[4] Metropolitan Asylums Board Report, p. 52.

[5] Ibid, p. 54.

overcoming this septic infection, and not with the idea of combating the causal agent of scarlet fever itself. We believe that this scarlet fever agent, whatever it may be, will die if the superadded septic infection is removed.

Excellent work has been done on the bacteriology of the normal nose and also of its inflammatory diseases. Our work is confined entirely to these cases of septic rhinitis complicating scarlet fever. We were surprised at first with the great regularity in which staphylococci were found, usually aureus, and practically in pure culture. We felt that possibly our technique was faulty and that some of the organisms might have escaped detection Accordingly the various methods and media which have been advised from time to time for isolation of streptococci, pneumococci, and the influenza and diphtheroid group of bacilli were employed. But, as wlll be seen, our findings include but four organisms: Staphylococcus aureus occurred alone in 89 cases; Staphylococcus albus in 3 cases; a diphtheria-like bacillus in 6 cases; Staphylococcus aureus and a diphtheria-like bacillus occurred together in 1 case; and Staphylococcus aureus and Streptococcus pyogenes were found associated in 1 case.

The staphylococci and Streptococcus pyogenes were isolated and classified according to cultural and biological characteristics. Special attention was given the diphtheria-like organisms because of their relation to the Klebs-Loeffler and Hofmann's bacillus. As will be noted in the tables, they were found in 7 per cent. of the cases. In every instance the organism was of medium length, solid, with rounded or slightly pointed ends, evenly and darkly staining, Gram positive, and in four instances showing a faint median band. Unfiltered bouillon cultures and filtered toxins grown for forty-eight hours were made and injected subcutaneously into guinea-pigs in doses corresponding to 0.5 per cent. of the body weight of the animal expressed in cubic centimeters. All gave negative results. Three cultures were inoculated into tubes containing Hiss serum water media containing 1 per cent. of dextrin, maltose, mannite, lactose, and saccharose respectively. In one case acid was produced in dextrin and maltose, indicating the true diphtheria bacillus, the other two yielded negative results, indicating Hofmann's bacillus.

The following table gives the duration of the septic rhinitis prior to culturing and the first dose of bacterin:

| | Cases. |
|---|---|
| Two to four days | 48 |
| Four to seven days | 19 |
| Seven to twelve days | 16 |
| Twelve to twenty days | 6 |
| More than twenty days | 11 |

Cases of nasal discharge were reported to us on the second or third day of discharge. The case was then examined and the ques-

tion of the advisability of bacterin treatment considered. A culture was then made, and in a large number of cases a dose of stock polyvalent Staphylococcus aureus vaccine was administered at once. In many cases this was the only dose required, but all cases were cultured in order to detect the presence of some organism other than the Staphylococcus aureus. If two organisms were found they were isolated and a separate bacterin of each prepared. The aggregate dose of the two bacterins equalled the usual dose of one. The size of a dose depended upon the general condition of the patient; the younger and weaker receiving correspondingly smaller doses. The initial dose varied from 50,000,000 to 100,000,000 of staphylococci and 50,000,000 to 80,000,000 of the diphtheria-like organism. Succeeding doses were given every five to eight days, depending upon the clinical aspect of the patient. Injections were given in the loose areolar tissue of the back by means of an all-glass sterilized syringe. All other treatment was stopped except cleanliness of the parts and application of soothing ointments. Other infections, toxemia with fever, nephritis, and low vitality were considered contraindications. The following table gives the number of doses administered, with the results obtained:

| Doses. | Cases. | Cured. | Improved. | Not improved. | Other infections. |
|---|---|---|---|---|---|
| 1 | 43 | 39 | 1 | 2 | 1 |
| 2 | 29 | 23 | 3 | 1 | 2 |
| 3 | 12 | 9 | 1 | 2 | |
| 4 | 6 | 3 | 1 | 2 | |
| 5 | 6 | 2 | 2 | 2 | |
| 6 | 3 | 1 | .. | 2 | |
| 7 | 1 | .. | .. | 1 | |

The temperature reaction following the injection was moderate, reaching 100° to 102° F., and falling to normal in twenty-four to thirty-six hours. We never had an abscess. There is usually a slight local redness and tenderness and general malaise following the injection. In the majority of cases the discharge begins to lessen after twenty-four hours. The congestion of the turbinates was relieved quite promptly, and in two to four days bad cases were well. If no improvement followed three doses, another culture was made and a bacterin prepared. Examination was also made for the presence of adenoids. If these were present, bacterin treatment was stopped, as treatment in such cases has proved to be valueless. In the first few cases of adenoids, extensive treatment was persisted in, but to no avail. All cases were retained in the hospital from four to ten days after the rhinitis had cleared up.

It is a difficult matter to draw an impartial conclusion concerning the value of bacterin treatment in these cases of septic rhinitis. In individual cases the results were most striking, when we naturally expected a prolonged course would follow under ordinary treatment. This rhinitis occurs in from 10 to 20 per cent. of cases and is usually persistent. Many cases heal promptly with usual

treatment, but the time required for such a result is very much decreased with bacterin treatment. We have not been able to trace one "return case" which can be attributed directly or remotely to one of the cases that received bacterin treatment.

Examination of the last table shows a cure in 77 per cent. of cases; 8 per cent. were improved, 12 per cent. not improved, and 3 per cent. contracted other infections, and the treatment was stopped. The 8 cases showing improvement had a very slight discharge when dismissed; 9 of the cases not improved had adenoids, and 3 were of poor vitality; 1 patient developed pertussis, 1 Vincent's angina, and 1 acute scarlatinal nephritis. All cases not cured were held at least four weeks over the usual period of residence in the hospital.

For the sake of comparing the efficacy of stock and autogenous bacterins, about an equal number of cases were treated with each. The stock bacterin was made from twelve different cultures of Staphylococcus aureus. All bacterins of the diphtheria-like bacillus and the Streptococcus pyogenes were autogenous.

| Cases treated with | Cured. | Improved. | Not improved. | Other infections. |
|---|---|---|---|---|
| Autogenous bacterins, 52 . . | 35 | 6 | 10 | 1 |
| Stock bacterins, 48 . . . | 43 | 2 | 1 | 2 |

All the adenoid cases were treated with autogenous bacterins, which accounts for the apparently better results with the stock bacterins. The results were about equal.

Conclusions. 1. That nasal discharges are of primary importance in the etiology of the "return case" of scarlet fever.

2. That the true rhinitis of scarlet fever is septic in character, distinctly infectious in itself, and probably harbors the contagium of scarlet fever.

3. That bacterin treatment of cases of septic rhinitis is more satisfactory than the usual treatment. It shortens materially the time required for cure and decidedly aids in decreasing the number of "return cases."

## CHRONIC PNEUMONIA (INCLUDING A DISCUSSION OF TWO CASES OF SYPHILIS OF THE LUNG).

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Among the numerous indurative processes in the lung, chronic (unresolved, organizing, or indurative) pneumonia is specially interesting from the high frequency of complications, and especially on account of the irregularity of its clincial symptoms and the

uncertainty of its diagnosis and prognosis. Owing to this uncertainty, the diagnosis is, it might be said, as a rule, mistaken, and it also perhaps accounts for the rather incomplete clinical data relating to this disease.

Of a series of 159 cases of pneumonia which came to autopsy in the Russell Sage Institute, New York (95 lobar and 65 bronchial), 10 (6 males and 4 females) illustrated examples of this organizing type. In 9 of these, whole lobes or at least large areas of the lung were affected, and in only 1 was the process more patchy in character and more definitely bronchopneumonic in distribution.

These 10 cases represent examples of pneumonia where the usual process of resolution has failed and organization of the inflammatory exudate in the air alveoli of the lung by fibrous tissue has resulted.

Such conditions of non-resolution and fibrous organization of acute pneumonic processes have been recognized as a clinical and pathological entity for some considerable time, particularly by German writers; yet in English literature it has occupied only a relatively slight interest, either as regards its clinical importance or its pathological distinctive features. Laennec[1] in 1819 was perhaps the first to observe this type of disease. He considered that the lung presented in these cases a greater hardness, was more regular, and a more gray-violet, livid red color than in simple hepatization. Andral in 1837 described somewhat similar appearances, and Stokes in 1838 noted definitely a case of pneumonia as having become chronic after one month's duration of the acute condition. Lebert[2] in 1857 spoke of a "transformation fibreuse" of the pneumonic exudate, and Rokitansky in 1861 advocated the possibility of a simple hepatization becoming hardened into an "indurierte Hepatisation" and also of "neugebildeten Bindegewebes-elementen welche den Elementen des Eiters und den aus den Eiter und Epithelial-zellen hervorgegangen Fettkörnchenzellen bei der Hepatisation oder eitrigen Infiltration beigemischt sind." In the text-books of Birch-Hirschfeld (1877), Jurgensen (1878), and Niemeyer-Seitz (1879) the possibility of a sequence of an "interstielle Pneumonie" after the acute croupous form is admitted. Virchow demonstrated the process of induration to be a vascularization and organization of the exudate, and applied the term "carnification" to the result ("Die Form der Induration welche die Alveolen ausfüllt, als Carnification").[3] Corrigan described "cirrhosis pulmonum" as a special disease, *sui generis*, analogous to liver cirrhosis, and Clark[4] came to a similar conclusion, noting also that "all cases of fibroid phthisis were not due to tubercle." Rindfleisch, Amburger,[5] and Hanau[6] were of the same opinion, as also was Balzer,[7] who described this special process as a "pneumonie chronique recurrente." Heitler[8] agreed that this chronic pneumonia was a distinct entity, and was developed from a "paren-

chymatous pneumonie." Buhl also strenuously denied any relationship to any acute condition, and he believed it commenced as a "desquamative pneumonia," and that, as regards croupous pneumonia, only capsulation or cicatrization around abscesses or gangrene was possible. Wagner[9] was not so definite, as he admitted the connection between acute and chronic pneumonia, but was not sure of any relationship between acute croupous pneumonia and the chronic indurated condition. Borrmann[10] also considered it risky to think of every case as arising as a special process and not as a sequence of acute pneumonia. Heschl,[11] Woronochin, Ackerman,[12] Eppinger,[13] and the majority of more recent authors, Leyden,[14] Lindemann,[15] Kidd,[16] v. Kahlden,[17] Aldinger,[18] etc., have followed Marchand[19] in his views that these cases of organizing pneumonia are sequels of an acute pneumonic process, and an event which may follow the acute croupous form ("das eine nachfolgende frische, croupöse Pneumonia, denselben Ausgang in Induration nimmt").

A variety of explanations have been advanced as to why this organization and not the usual process of resolution should occur in some pneumonia cases. Heschl has observed this transformation particularly in wasted individuals; Cornil and Ranvier and Marchiafava[20] found this type especially in very old, feeble subjects. Hart,[21] however, found well-marked organizing processes following bronchopneumonia associated with measles, and Ziegler described a similar event. Marchand considered it more frequent in alcoholics and Josephson[22] in alcoholic, defectively nourished subjects. Amburger advocated syphilis as the essential factor. Ziegler[23] considered the probability of recurring exudates eventually requiring organization for their removal, and Jurgenson that preëxisting congestion was of etiological moment. Eppinger and Cohn,[24] and to some extent Marchand, thought that pleural adhesions limiting the respiratory movements of the lungs and causing congestion were essential. According to von Kahlden,[25] obstruction of the bronchial tubes and resulting retention of unexpectorated exudate was important. Köster[26] showed the etiological importance of the lymph channels being clear if resolution is to take place successfully, and v. Kahlden has applied this to emphysema, where the walls of the air spaces are thin and their vascular and lymphatic channels naturally defective for absorption and resolution.

In a review of the 10 cases on which the present communication is based, it was seen that in 2 the pneumonic process was situated in the upper lobe of the right lung, one in the upper and middle lobes of the right lung, 1 in irregular patches throughout the right lung, in the middle lobe of the right lung, with extension into the adjacent upper and lower lobes, 1 in the lower lobe of the right lung, and 4 in the lower lobe of the left lung. These locations then do not conform to the common statement that apical pneumonias are specially subject to delayed resolution. With two exceptions all

the cases occurred between the ages of sixty and ninety-two years. In this connection, however, it has also to be noted that in the remaining 149 cases of pneumonia a similar proportion also occurred within about the same age limits.

The question of emaciation was also apparently of indifferent importance, as 4 of the cases were comparatively well nourished.

Likewise alcoholism, and certainly syphilis or tuberculosis, did not play an essential part, as in only 3 of the 10 cases was there any history of syphilis, and in 2 small healed foci of tubercles were found in the apices of the lungs.

Emphysema was considerably more important, yet the lungs in 7 at least of the 9 cases were only moderately emphysematous, and on microscopic examination the alveolar walls did not seem to be especially atrophied.

Nephritis and general arteriosclerosis were also in no degree constant, nor was there any special chronic cardiac condition or marked general venous stasis.

Eppinger and Cohn's ideas of the essential feature of pleural adhesion and thickening also could not be sustained, as in most of the cases there was no such fixation of the lung.

Occasionally some of the smaller bronchi were obstructed, but the process was coincident with the alveolar organization, and certainly did not necessarily precede it, as several authors have advocated.

One factor, however, as will be seen from the following synopses, was uniform in all the cases, that being their extreme debility, either from some preceding or coexisting disease.

CASE I.—An extremely emaciated man, aged sixty-eight years, who had entered the hospital in a state of extreme debility, and died shortly afterward. He had been confined to bed for about a month previously, but nothing further could be ascertained. The autopsy showed an organizing pneumonia of the lower lobe of the right lung, with also, as in all the other following cases an overlying subacute pleurisy.

CASE II.—A somewhat emaciated man, aged seventy-five years, who had suffered from dyspepsia due to carcinoma of the pylorus for seven months. At no time did he ever have any symptoms which might have been related to pneumonia. The temperature remained normal until the last four days of life, when it rose to 100°, and remained about this level. During the whole fourteen days in hospital there was dulness noted corresponding to the lower lobe of the left lung, and over this area faint bronchial breathing without any accompanying rales was heard. At autopsy the lower lobe of the left lung was consolidated and fleshy in consistence from organizing pneumonia.

CASE III.—A fairly well nourished man, aged sixty-five years, who entered hospital extremely debilitated, in the convalescent

state of facial erysipelas, which had started three weeks previously. Beyond this no definite history relating to pneumonia could be determined. On first examination his leukocytes numbered 16,500 per c.mm., and there was definite dulness and bronchial breathing over the middle lobe of the right lung. He lived twelve days after his admission to hospital, the temperature, at first 102.6°, continued to swing irregularly, with a maximum of 103°, and toward the end, as evidences of empyema developed, an incision was made just anterior to the right nipple, and a loculated pneumococcal empyema over the outer part of the middle lobe of the right lung was drained. At autopsy there was a small gangrenous patch in the middle lobe, which communciated with the empyema cavity. The rest of the middle lobe was in a condition of organizing pneumonia, as was also the lower part of the adjacent upper lobe.

Case IV.—A fairly well nourished man, aged sixty-three years, who presented an alcoholic history, and for the last thirteen years had occasional attacks of cardiac insufficiency and anasarca from chronic nephritis. Forty-two days before the date of his death, after two days' exposure in an alcoholic condition, he experienced sudden chills and pain in the left side of the chest. On his entrance to hospital ten days after the onset of these symptoms there was definite bronchial breathing, some fine crepitations, and fine friction rales over the lower lobe of the left lung. The leukocytes numbered 22,000 per c.mm. (82 per cent. polymorphs). Ten days later a pericardial friction rub became evident, and the heart's action assumed a gallop rhythm. The leukocytes at this time numbered 8000 per c.mm. The temperature had a daily range of between 102.5° and 99° as an average during the whole thirty-two days in hospital; the pulse averaged 100, and respirations 28 throughout. At autopsy there was an organizing pneumonia of the lower lobe of the left lung. The left pleural cavity contained a small amount of turbid fluid, from which pneumococci were isolated. The right pleural cavity also contained a small amount of clear fluid. There was also a fibrinous pericarditis, the pericardium containing a small amount of turbid fluid, in which pneumococci could be demonstrated, and the surface of the heart was entirely covered by a shaggy fibrinous exudate.

Case V.—A somewhat emaciated man, aged thirty-two years. When twenty years of age he had a chancre, but no secondary eruption. Seven years later he developed a gradually advancing hemiplegia, which was complete in three months. On admission to hospital he presented a complete right spastic paralysis, and his heart was markedly enlarged from aortic incompetence. During the six weeks he was in hospital the temperature remained normal, pulse averaging 80, and respirations 22. He did not complain of any symptoms referable to the respiratory system except some occasional fits of coughing. Twenty-one days before death, however,

a fine friction rub became evident over the upper part of the right interscapular region, and on deep respiration there was some catching pain over the upper part of the right side of the chest. No sputum was expectorated. Over the upper lobe of the right lung dulness and high-pitched bronchovesicular breath sounds developed. Two days before death he suddenly developed typical signs of meningitis. Coincidentally, the temperature, previously normal, rose to 105.5°, and the leukocytes rose to 32,000 (58 per cent. polymorphs) from a previous maximum of 14.500 per c.mm. Toward the end the hemoglobin had fallen to 58 per cent., and the red blood corpuscles to 3,597,000 per c.mm. At the autopsy the upper lobe of the right lung, with the exception of the extreme apex, was carnified from chronic pneumonia. The brain and spinal cord showed a marked purulent pneumococcal meningitis, the pus being chiefly aggregated over the vertex of the cerebrum. There was also an old atrophy of the left Rolandic area of the brain, due to old thrombosis, and the aortic valves of the heart were incompetent from chronic endocarditis.

Case VI.—A well-nourished woman, aged ninety-two years, whose only obtainable history was that she had been hemiplegic for some years, and had been latterally for some months confined to bed. Clinically the presence of fluid in the right pleural cavity was suspected, but the temperature, pulse, and respiration, although not fully recorded, were not abnormal until the last two days of life, when the temperature rose slightly. At autposy about 15 ounces of a thin fluid, from which a pneumococcus and staphylococcus albus were isolated, was found in the right pleura. There was an organizing pneumonia of the lower lobe of the right lung, and the organization in this case was comparatively advanced and fibrous. The pericardium contained a small amount of slightly turbid fluid, and there were patches of recent fibrinous deposit on the surface of the heart, particularly near the base. (As no organisms could be discovered in the pericardial exudate, it was difficult to establish the absolute relationship of the process). The kidneys (left, 150 grams; right, 115 grams) showed some arteriosclerotic atrophy, and there was an old thrombosis of the left middle cerebral artery, with atrophy of the convolutions of the Rolandic area and under surface of the temporosphenoidal lobe on the left side. In this case the duration of the pneumonic process was not determined, but evidently from the advanced state of the organization it must have existed for some considerable time.

Case VII.—A poorly nourished woman, aged sixty years, who had entered hospital complaining of cough and breathlessness, which had followed a severe cold contracted three weeks previously. During these three weeks she had been under the influence of alcohol almost continuously. Two days before admission

to hospital she suddenly became very feverish, and her breathlessness much more marked. When first examined in hospital there was an indefinite dulness, with harsh vesicular breath sounds and prolonged expiration, accompanied by numerous moist crepitations over the lower part of the left side of the chest. Over the upper lobe of the right lung there was definite dulness and fairly loud bronchial breathing. There was a soft systolic mitral murmur transmitted out into the axilla. The leukocytes numbered 24,000 per c.mm. (85 per cent. polymorphs), and the temperature was 102°, pulse 100, and respirations 34. The sputum was yellow, tenacious, and contained numerous pneumococci. The temperature gradually rose to 104° on the fifth day and came down by lysis to 100° on the eighth day. It varied between 100.5° and 99° for the next six days, when it again rose to 101.5° (sixteenth day), returning to 99° the next evening. At this period the leukocytes numbered 32,000 (83 per cent. polymorphs). The temperature continued varying between 99.6° and 98.2° until the twenty-first day, and since then until the twenty-eighth day, when death occurred suddenly, the temperature remained within normal limits. During the whole time in hospital the respirations averaged 26 or 48 per minute and were not particularly labored. At autospy it was found that the lower lobe of the left lung was edematous, congested, and bound down by numerous stringy adhesions. The lower two-thirds of the upper lobe of the right lung showed an organizing pneumonia, and over its surface was a subacute pneumococcal pleurisy. The pneumonic area was fleshly in consistence, dark brownish red in color, and included numerous grayish streaks and spots. The pericardial sac was separated from the heart by a thick layer of creamy pus, in which numerous pneumococci were demonstrated.

Case VIII.—An emaciated male, aged seventy years, who had come to hospital for a severe ulcerative stomatitis. He was not specially alcoholic, and he denied any previous illnesses. At this time his lungs were reported as generally emphysematous. Two months later he developed double otitis media, for which a radical mastoid operation was performed on the right side. The temperature, which had developed with the onset of the middle ear disease, continued irregularly, varying between 100° and 102° for ten days after the operation. Six weeks later (four days before death) the temperature again became irregular, reaching up to 102°, but falling the next day to 97°, and remaining until the end at about 99°. At no time was the pulse or respiration rate apparently altered from normal, and he presented no symptoms relating to his respiratory system. The diagnosis of pneumonia was not made, and he died in extreme asthenia, having emaciated very markedly in the last month.

At autopsy both middle ears and mastoids were filled with a large amount of greenish-yellow pus, containing staphylococci and

streptococci, and from the right mastoid a sinus communicated externally. There were numerous encapsulated trichinæ in the chest and abdominal muscles. No fluid was contained in either pleura. The lower lobe of the left lung was fleshly in appearance, from organizing pneumonia, and over its surface was a thin patchy layer of subacute pleurisy. Throughout the pneumonic area in this lung were numerous miliary abscesses.

CASE IX.—An emaciated man, aged sixty-eight years, who had an alcoholic history, and who had entered hospital complaining of dizziness, cough, and defective vision. Two days later the temperature slowly rose to 101°, and next day reached 104.4°. At this point he became wildly delirious, and continued so for the next ten days, the temperature during this time varying between 101° and 103°. Respirations averaged 28 and pulse 120. During the following six days the temperature ranged between 99.5° and 101° and during the succeeding week, at the end of which he died, the temperature had again risen, varying irregularly between 99° and 103°, and without the pulse or respiration becoming altered appreciably. The day before he died the leukocytes numbered 23,200 (82 per cent. polymorphs), the red blood corpuscles 3,472,000, and the hemoglobin 60 per cent. Throughout his illness, aortic incompetence was diagnosticated, but no condition of pneumonia was determined. His chest, however, could not be fully examined, on account of his delirium, although it was noted that the chest was hyperresonant throughout on first examination, and toward the end there was a slight dulness at the lower part of the left side of the chest. At autopsy 50 c.c. of thin pus, from which pneumococc were isolated in pure culture, was found in the left pleura. The left lung was congested and edematous, but contained no pneumonic areas. The right pleura was universally adherent. The right lung was somewhat emphysematous, and showed a whitish firm area of chronic organized pneumonia, about ¾ inch in diameter, and a similar grayish, firm, non-friable patch, 1½ by 2½ inches toward the lower part of the upper lobe corresponding to the axillary region. There were also several small, firm, more reddish areas in the upper part of the lower lobe of the right lung. These, however, did not resemble infarcts in any stage nor any tuberculous or syphilitic process, and microscopically they were proved to be areas of organizing pneumonia in which the inflammatory exudate in the air alveoli were penetrated or even replaced by loops of granulation tissue extending from the alveolar walls.

CASE X.—A large, well-nourished, plethoric-looking male, aged forty-three years. He had been an extremely heavy drinker, and gave a history of a sore on the penis, but no secondary symptoms. For several years he had been troubled with shortness of breath, but never had noted any edema. Three months previous to his entrance to hospital his friends informed him that he was jaundiced. Since

that time he emaciated rapidly and the jaundice deepened. Twenty-three days before admission, after he had been working around in a snow-storm, he had a severe chill, followed by high fever. Next day he felt catching pains in the right side of the chest, and became short of breath. He remained in this feverish condition until he came to hospital. On first examination there was noticed to be a moderate degree of jaundice, and the liver was readily palpable and slightly enlarged. The spleen extended 2½ inches below the costal margin. The heart was dilated, and there was a soft systolic murmur best heard at the apex. The urine contained a considerable trace of albumin, and was passed in considerable quantity. The chest was barrel-shaped, and over the upper part of the right side there was a decided limitation of movement. In this situation over the upper and middle lobes, there was distinct dulness on percussion, and the breath sounds were high pitched and definitely bronchial. There were crepitations all over both lungs, much coarser over the right upper lobe. The temperature was 102.5°, respiration 36, pulse 126, blood pressure 135. The leukocytes were estimated at 40,000 per c.mm. (86 per cent. polymorphs); red blood corpuscles 4,248,000; hemoglobin 65 per cent. Six days later the jaundice remained the same, and the temperature continued irregulary raised to a maximum of 103.5°. The leukocytes were estimated at 35,000 per c.mm. (85 per cent. polymorphs), but two days later dropped to 26,800 per c.mm. He died in an extremely asthenic state fifteen days after his entrance to hospital, and on the fortieth day since the onset of his febrile symptoms. Until the end the temperature varied irregularly between 101° and 103.5°, and two days before death the leukocytes numbered 35,600 per c.mm. Dulness over the right upper and middle lobes persisted to the end, but the breath sounds over this area became rather fainter. During the last three days some dulness became evident over the left upper lobe, and during the last week ascites had developed, and rapidly increased. The presence of peritonitis was unsuspected, as he complained of no pain, nor was his abdomen specially rigid.

At autopsy the peritoneal cavity was found to be filled with a large amount of turbid fluid, which on microscopic examination was observed to contain numerous pus cells and pneumococci. The liver was in a condition of fatty coarse cirrhosis. The pleura on the left side was completely obliterated by adhesions, and the middle lobe and lower part of the upper lobe were involved in a process of organizing pneumonia, being dark reddish gray in color and fleshy in consistance. The upper lobe of the left lung was congested and slightly collapsed apparently by the action of the heart being pressed upward against it by the collection of fluid in the abdomen. It also presented quite a different appearance from the pneumonic condition in the right lung.

In such debilitated states as is illustrated by these cases, it is natural to assume a defective absorption of the exudate from the inflamed alveoli, and of course the patency and absorptive power of the lymphatics, as Koster suggests, is also naturally of the first importance.

As regards the miminum time necessary to produce a chronic pneumonia from the acute process, Ziegler places it at ten weeks, McCrea[27] at twenty-two days, and von Kahlden considered that any case persisting after fourteen days to five weeks would show organizing processes. In several cases which I have seen, where the pneumonic process seemed clinically to last as long as thirteen to fifteen days, the lungs at autopsy showed a condition of gray hepatization, but no organization. Fourteen days is possibly rather a low limit. In the ten cases here recorded the shortest duration was twenty-three days, but as was evident from the clinical histories, exact durations are in many cases impossible to determine.

The question of the type of the exudate into the air alveoli has also to be considered in relation to the occurrence of delayed resolution by organization. For instance, in pneumonia the exudate may be specially fibrinous, or it may contain an unusual number of leukocytes. Is this delayed resolution process then due to a defective emigration of leukocytes which do not remove the foreign material in the air spaces, as is usual by their vital action of phagocytosis, enzyme secretion, and solution, or is it, as Flexner[28] concluded, due to defective cellular content in the exudate and consequent failure of the autolytic processes of enzyme formation and fibrin solution which are known to follow on the death of cells and so necessitate the development of processes of organization? In relation to this latter view, however, if one might judge from the numerous evidences of cellular activity in pneumonia, resolution is more of the nature of a vital process and the removal of the exudate is by phagocytosis and active enzyme secretion, and is finally completed by absorption into the lymphatics of the alveolar walls.

In the present series of cases of delayed resolution pneumonia no special type of cellular exudate could be determined, chiefly from the difficulty of correctly reconstructing the process on account of the advanced age of the disease. The exudate into which the granulation tissue penetrated, consisted chiefly of rather small mononuclear cells, loosely aggregated, and generally surrounded by some loose fibrinous debris. Occasionally these mononuclear cells were relatively very large, and contained some blood pigment, but hemorrhages into the air alveoli were not particularly common. Plasma cells, as might be expected, were sometimes to be seen, but polymorphonuclear leukocytes were distinctly rare.

It is quite probable that there is a failure of leukocyte emigration or activity, and consequent defective bacterial destruction and

solution of the inflammatory exudate, or an insufficient proliferation or phagocytic activity of the lining cells of the air alveoli. Yet this was by no means easy to substantiate in these cases. It has, moreover, to be remembered that in most of the cases a continuous temperature, more or less, prevailed, and thus one might presuppose a continued infection of the air alveoli, and eventually as a necessary consequence the replacement of the renewed inflammatory exudate by organization.

The source of the indurating tissue in the lung in these cases has provided some considerable speculation. Ackermann and Thier-

FIG. 1.—Case IV. Organizing pneumonia. The majority of the air spaces are almost completely filled with masses of fibrous tissue. × 65.

felder have considered the ingrowth of fibrous tissue into the alveoli as derived from the interlobular septa, and Eppinger and Cohn have advocated an extension from the peribronchial tissues as the essential factor in the induration. Heschl (1856), Woronochin (1868), Marchand (1880), Lindemann (1888), Cox[31] (1889), Rieder[32] (1890), Borrmann (1896), v. Kahlden (1987), etc., have all shown the origin of the new granulation tissue from the alveolar walls themselves.

In all the cases the process seemed to be much the same. The affected portion of the lung was practically airless, fleshy in consistence and in color, with the exception of two cases, where

it had a pale grayish-pink appearance. The overlying pleura was not specially thickened, nor was there any evidence of gross cicatrization in the pneumonic areas. On microscopic examination there was originally in all, apparently, an acute pneumonic exudate, which, in varying degree, was being organized by projection of granulation tissue from the alveolar walls, into the inflammatory exudate (Figs. 1 and 2). Some of the infundibular spaces and bronchi underwent a similar organizing process (Fig. 3), yet obviously this was not the initial condition. The air spaces were, as a whole, not particularly emphysematous, and the outlines of the alveoli, even although the whole air space was filled by organizing tissue, could still be, as a rule, easily

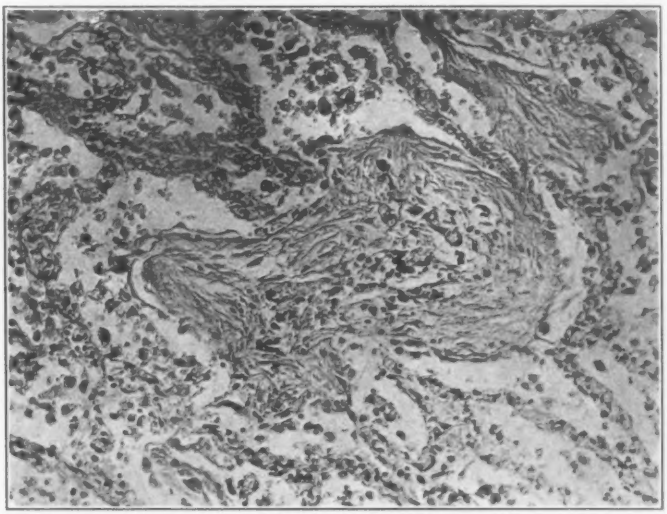

FIG. 2.—Air alveolus, showing organization of its inflammatory content. × 185.

determined, and did not appear disintegrated. The capillaries in the alveolar walls were generally somewhat congested, but stasis was not a marked or constant feature. The elastic-tissue structures of the alveolar walls were sometimes fibrillated, as is found in any case of pneumonia, and often irregular degenerated fragments of this elastic tissue could be seen among the granulations penetrating into the air spaces. No new formation of elastic tissue was found in the invading organization tissue in any case. For the most part the organization of each lobule was an individual process, yet frequently also an extension through from the adjacent lobules were observed. Organization usually took place as a projection from one or only a few foci on the alveolar walls. The extent of this

organization, of course, varied in the different cases, as in some the greater number of inflamed alveoli were penetrated and filled to a greater or less extent with the new fibrous tissue, and in others relatively few of the alveoli were involved in the organizing process. In one case, VIII, there apparently had been a more severe infection, and consequently a greater destruction of lung tissue, as in may places the sprouts of granulation tissue had become confluent (Fig. 4).

Tubercle bacilli and spirochetes were searched for in all the cases, but in none of them were any discovered.

FIG. 3.—Case IX. Chronic pneumonia. Organization of inflammatory content in the ria alveoli and small bronchioles. × 100.

A great variety of conditions, of course, lead to induration of the lung, such as tuberculosis, pneumokoniosis, cicatrization around gangrenous areas or abscesses, but none of these closely simulate this condition of chronic organizing pneumonia.

Extension of fibrous tissue from the pleura is not a definite process, although the pleura is naturally a source from which scar tissue may be derived in the process of repair of damaged areas in the lung. Pleurisy itself does not usually extend its inflammatory process far into the lung (Fig. 5), and if any extensive fibrosis

in the lung is in connection with the pleura, it means the result of some irritative destructive or pneumonic process in the lung itself.

Cyanotic induration also has never the appearance of an organizing pneumonia either grossly or microscopically (Fig. 6).

Atelectasis of the lung, however, has grossly, in some cases, a close resemblance to the "carnified" appearance of an organized pneumonia. In collapse, however, the marked shrinking in volume, with the consequent aggregation of bronchi and vessels, provides some little distinction. A microscopic examination of 26 cases of

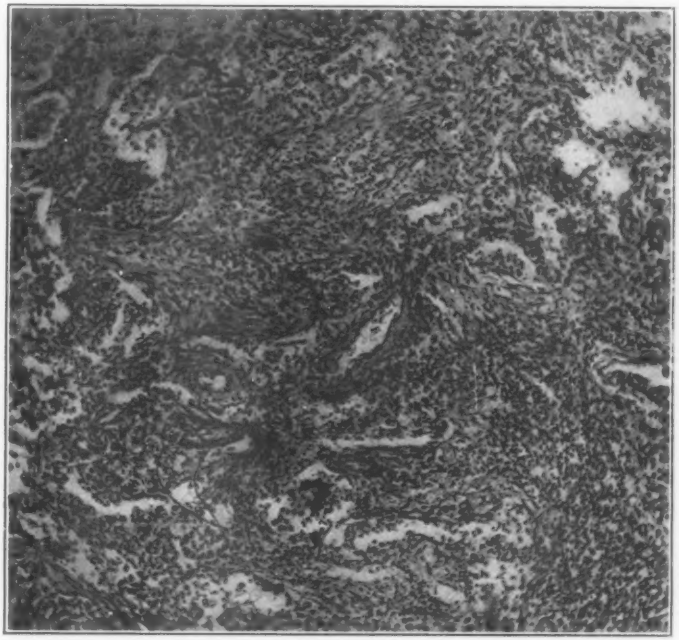

FIG. 4.—Case VIII. Organising pneumonia. The air alveoli are extensively invaded by granulation tissue, but in many parts the walls are destroyed. In certain parts small abscesses are also evident. × 100.

old-standing collapse, resulting from the pressure of fluid in the pleural cavity, emphasized the distinction between this condition and pneumonic processes. To produce a complete collapse it requires a large amount of fluid exerting its pressure for some considerable time. The air alveoli may become so compressed that the walls may actually come in contact with each other, so that the whole tissue comes to resemble a mass of capillaries (Fig. 7). Usually, however, the lining cells become swollen, and thus what at first sight looks like a solid fibrous tissue is found to be a mass of

capillaries, including small collections of darkly staining small mononuclear cells, which once constituted the flattened lining epithelium of the air alveoli (Fig. 8). The interalveolar septa do become thickened, but on close examination it is surprising how little real fibrous overgrowth has occurred. Several authorities, however, such as Feustell,[33] have considered that in collapse there is an extensive fibroid development and Berlin[34] thought that even bronchiectasis might be produced by collapse and cyanotic induration. In some cases of old-standing collapse the quantity of

FIG. 5.—Chronic pleurisy, showing extension of chronic inflammatory tissue into the lung from the pleura. The lining epithelium of the air spaces included in the fibrous tissue has become swollen and adenomatous in appearance. × 100.

elastic tissue is apparently enormous (Fig. 9); yet on reconstructing this it is found that it is merely the normal alveolar elastic fibrils aggregated, fibrillated, and swollen up. A distinction between collapse and organized pneumonia had to be made in Case V, where there was about a liter of pus in the left pleural cavity. All the evidences, however, in this case—clinical, anatomical, and histological—determined in favor of a pneumonia. These conditions of organizing pneumonia, which are naturally associated with considerable congestion of the lung, may also occasion an effusion of fluid into the pleura, and thus again, unless carefully distinguished, become confused with collapse. Another example

may be noted where a mistaken autopsy finding was corrected microscopically, and by the clinical history. It occurred in a man, aged thirty-eight years, who had come to hospital for symptoms of cardiac failure, secondary to aortic incompetence. He developed signs of fluid in the right pleural cavity twenty days before death, but his temperature and respiration remained unchanged. Four days before death a typical lobar pneumonia of the right upper lobe set in, and the temperature rose to 103.8°, and remained about that level until just before death, when it fell to 97.2°. His leuko-

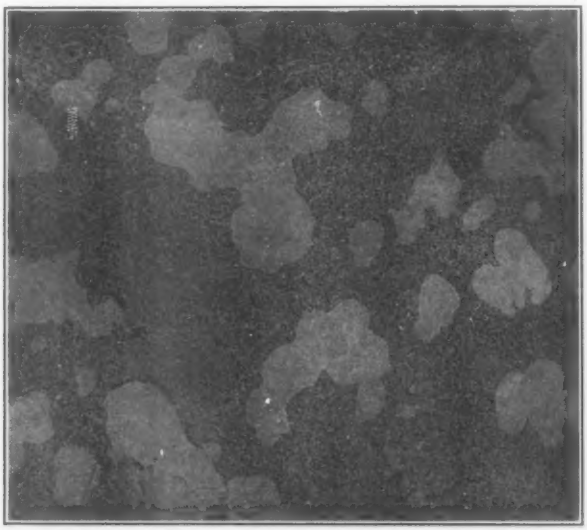

FIG. 6.—Cyanotic induration of the ung from a case of mitral stenosis in a boy. The interalveolar tissues are extensively thickened and infiltrated by new connective tissue. These thickened septa, however, contain congested vessels whose walls are thickened and some small alveoli completely filled with catarrhal cells and blood. The air spaces are occasionally filled with an edematous fluid or blood, but many are empty and lined with a flattened epithelium. There is no noticeable organization of the contents of the alveoli. × 75.

cyte count rose from normal to 20,000 (96 per cent. polymorphs), respirations changed from 23 to 44, and the pulse rate from 72 to 128.

At autopsy there was some thin, turbid pneumococci containing serous fluid in the right pleural cavity. The upper lobe of the lung was completely consolidated, showing a beginning gray hepatization. The lower lobe, particularly in its lower two-thirds, was dark brown, and fleshy in appearance. There was some considerable reduction in size, yet it seemed like an organizing pneumonia. This impression was, however, corrected on microscopic examination, as the usual

features of a collapse were demonstrated without any of the appearances of an organization of an inflammatory exudate.

Another case in which a mistaken diagnosis of organized pneumonia was made at autopsy was also of some interest. It occurred in an emaciated female, aged seventy years, who had died from asthenia consequent to a cancer of the head of the pancreas. There were numerous metastases along the lesser curvature of the stomach, involving both suprarenals, around the neck of the gall-bladder, in the liver, and in the retroperitoneal mesenteric mediastinal and bronchial glands. No metastatic involvement of the lung

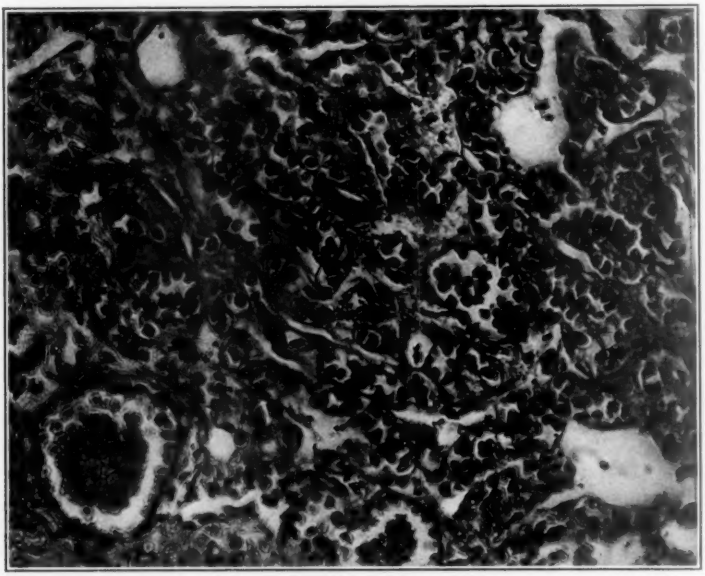

FIG. 7.—Collapse of lung, following pleurisy, with effusion. The alveolar wall capillaries are distended and crowded together. × 400.

was evident grossly. The middle lobe of the right lung, and also for a short distance above and below this, appeared firm, dark brown red in color, and traversed by a few fine, irregular, fibrous-looking streaks. This was considered to be an organizing pneumonia, but on microscopic section it was found to be a very diffuse cancerous invasion. Considerable portions of the lung tissue were exclusively occupied by the newgrowth, and in many parts also the air alveoli appeared filled with tumor cells. These alveoli, which were not invaded by cancer cells, were filled with an inflammatory content, nd there was also considerable inflammatory reaction in those into which the cancer elements had penetrated.

The other condition which presents features closely resembling chronic pneumonia, and with which in the past many cases have been classified, is the effect of syphilis on the lung.

At the present time, in spite of the great prevalence of syphilis and of syphilitic processes in other organs, lesions produced by it in the lung are of comparatively rare occurrence. An extensive literature has accumulated, as in older literature, syphilis of the lung occupied a much wider sphere and more important clinical interest.

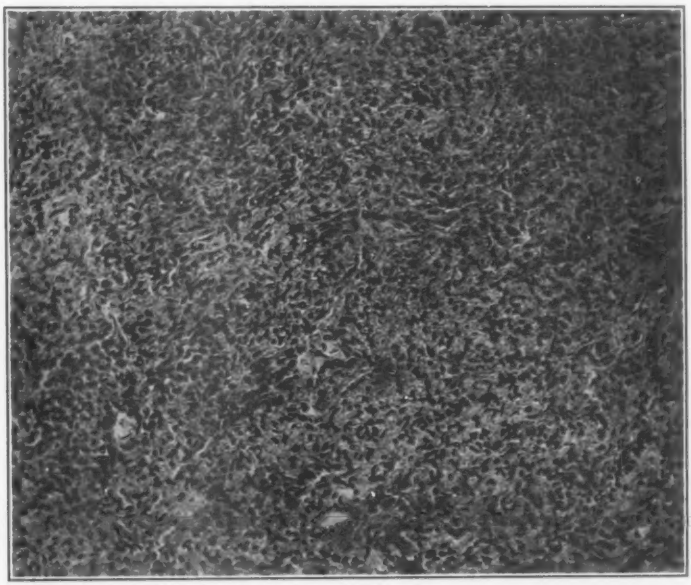

FIG. 8.—Collapse of lung, following pleurisy, with effusion. At first sight this tissue appears almost wholly fibrous, but on high-power examination the outlines of the alveoli can readily be determined. The alveoli are crushed together and their lining cells are swollen, giving thus the cellular appearance to the section. × 150.

Such authors on pulmonary syphilis, such as Peter Pinctor (1499), Paraselcus (1491-1541), Cesalpini (1601), Boerhaave (1668-1738), and Astruc (1684-1766), did not combine with the term "syphilis of the lung" any description of a specific lung disease, but only observed that following luetic disease there was a disposition toward phthisis. From the descriptions of Depaul in 1853 and then of Hecker, Ricord, Dietrich, and especially Virchow,[35] syphilis of the lung has become recognized, as in other organs, as a definite anatomical process. Wagner,[36] Calomiatti,[37] Carlier,[38] Hiller,[39] Heller,[40] and many others have described apparent syphilltic involve-

ment of the lung. More recently, however, as syphilis of the lung has become more thoroughly understood and differentiated, there have been comparatively few works on the subject. Among these latter, perhaps the most comprehensive are by Flockman,[41] Herxheimer,[42] and Brandenberg.[43]

The following two cases, although illustrating only one type of syphilis of the lung, are of some interest in affording a basis of comparison and contrast with the organizing processes following acute pneumonia:

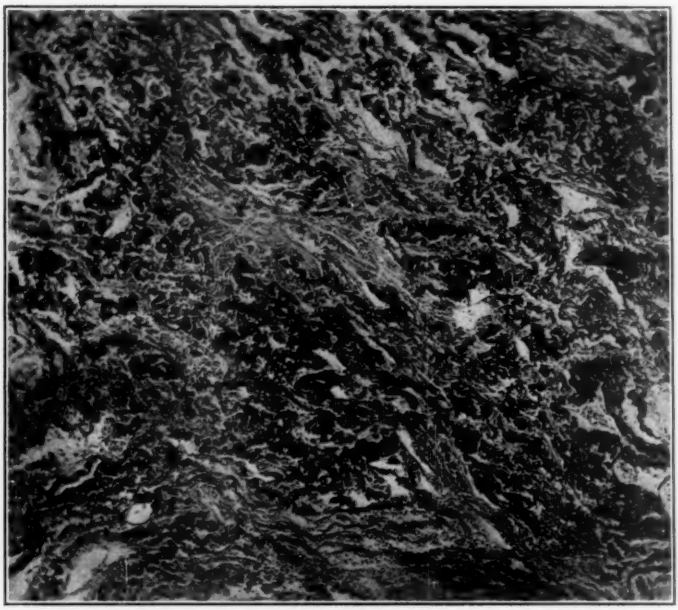

FIG. 9.—Collapse of lung, following pleurisy, with effusion. This is stained by Weigert resorcin-fuchsin method, and shows the apparently enormous amount of elastic tissue in such conditions. × 100.

Case I occurred in a fairly well nourished man, aged seventy-seven years, who had died from chronic nephritis and cardiac failure. The condition of his lungs during life had not disclosed any signs which had given rise to a suspicion of syphilitic fibrosis. At the autopsy no scarring of the skin, glandular enlargement, or other superficial signs indicated syphilis. Both pleural cavities contained a small amount of blood-stained serous fluid, and numerous stringy adhesions attached the lung to the chest wall posteriorly and laterally on both sides. The lungs were very emphysematous and anteriorly completely overlapped the heart. Over the lower lobes

the pleura was considerably thickened, and throughout both lower lobes, but particularly toward their bases, was a thick network of dense, well-defined fibrous tissue. There were no gummatous nodes, nor were there any large areas of fibrosis, although the strands of fibrous tissue varied considerably in thickness. Microscopically the fibrous tissue bands were fairly well defined, and were formed of old, dense, fibrous tissue. At the margins of this scar tissue there were, in places, small collections of anthracotic pigment, and in its interior remnants of included air alveoli were occasionally to be observed. The fibrous overgrowth was not particularly vascular, and its vessles were well formed and showed no perivascular lymphocytosis or obliterative endarteritis. There was no acute pneumonic or organizing process in the adjacent air spaces, and only a moderate degree of chronic venous congestion. No histological evidences of tubercle and no tubercle bacilli were to be observed. Spirochetes also, after repeated efforts, could not be demonstrated. There was some slight atrophic bronchitis, and the bronchial glands were small and atrophic. The larynx and tongue showed no particular change. The other organs presented no definitely syphilitic lesion. There was extensive general arteriosclerosis and considerable arteriosclerotic atrophy of the kidneys. The heart (650 grams) was dilated, and the myocardium of the left ventricle markedly hypertrophied, and the aortic valve segments sclerotic and incompetent.

Case II occurred in a somewhat emaciated woman, aged forty-four years, who had come under observation for constant headache which she had complained of for seven years and for pain and weakness of the legs during the last year. She presented the usual signs of tabes dorsalis, such as absence of the knee jerks, loss of pupillary light reaction, and optic atrophy. Her memory had lately become much impaired, and she was supposed also to have commencing general paresis. She had three children, all of whom died in infancy, but there was no history of miscarriages. She did not remember to have suffered from any previous illnesses, and denied venereal disease. She admitted, however, to have been in the habit of drinking five or six whiskys a day for the past fifteeen years. During the entire two months she was in hospital her temperature was somewhat irregular, every fortnight or so rising up to between 102° and 103.5°, and coming down by lysis in about six or seven days. For the last six days there had been another rise, but only to 100°, between which and 98° it varied until the time of death. There had, however, throughout been a slight cystitis, bacteria, and pus cells being passed in the urine. The urine, as a rule, was alkaline, of low specific gravity, and contained always a small amount of albumin and some granular, hyaline, and epithelial casts, and occasionally, expecially latterly, some blood. The thorax was symmetrical, large, and expansion fair. There was apparently no

abnormality on percussion, beyond some slight indefinite dulness at both bases; the vocal fremitus was noted as unimpaired. The breath sounds posteriorly were particularly feeble, and there were generally a few subcrepitant rales at both bases. The heart's apex was not palpable, but the outline of the heart was somewhat enlarged. There was a soft, systolic aortic murmur, which, however, was not transmitted far into the neck. The second aortic sound was markedly accentuated. Ten days before death she had an epileptiform convulsion and began to complain of severe headache, and since then was dull and irritable. Six days before death, coincident with a slight rise of temperature to 100°, she developed a cough, and there appeared an area of dulness over the upper part of the right lung, evidently from pneumonic consolidation. During the last two days of life she had almost continuous convulsions. The skin was dry and the bowels obstinately constipated. Pericarditic friction also developed at this time. Death apparently occurred from uremia.

At autopsy a considerable depression of the bridge of the nose, and numerous white, rounded scars, surrounded by a zone of brown pigmentation on the legs and abdomen, were observed. There was a large oval scar on the forehead the size of a silver dollar, and a large granulating ulcer discharging pus was situated on the upper part of the right thigh, but this did not apparently extend deeper than the subcutaneous tissue. Some of the scars were probably due to pediculosis, yet the majority were definitely of syphilitic origin. No general lymphatic glandular enlargement was noticeable. There was no fluid in either pleural cavity, and both lungs were densely adherent to the chest wall and to the pericardium. The lungs were somewhat emphysematous, completely covering the heart anteriorly.

The left lung on section, as a whole, was emphysematous and congested. In the lower lobe there was a dense network of fibrous tissue, particularly condensed at the lower anterior portion. About one inch from the lower outer margin was a large white cicatrix extending into the lung from the pleura for a considerable distance, and several other smaller scars also extending into the lung in other positions in the lower lobe. In the upper part of the lower lobe the fibrous network was more delicate and slightly pigmented. In the upper lobe there was practically no fibrosis. In the lower lobe between the meshes of fibrous tissue, and extensively in the upper lobe, were numerous large, friable, granular-looking areas of apparently gray hepatization pneumonia. Toward the apex these pneumonic areas were more or less confluent. In the lower lobe about the centre there was a circular abscess, about one-half inch in diameter, with rather ill-defined outline, and surrounded by a narrow congested zone.

The right lung was somewhat similar, a dense, fibrous network

pervading the lower lobe, particularly in its extreme lower part (Fig. 10). About the centre of the outer and extreme lower part of the lung there was a square-shaped area, about two inches in transverse diameter and one inch vertically, composed almost completely of dense fibrous tissue, and just above this a long, thick, fibrous scar extended for a considerable distance from the pleura into the interior of the lung. The upper and middle lobes were comparatively free from this fibrosis. As in the left lung, there were numerous acute bronchopneumonic patches, which in the upper part of the upper lobe were confluent. Several small acute abscesses were found in the interior of the lower lobe in its upper and middle portions.

FIG. 10.—Syphilis of lung. Lower lobe extensively infiltrated by syphilitic cicatricial tissue.

Microscopically, the fibrous meshwork in the lungs was found to be composed chiefly of dense fibrous tissue. This fibrous tissue, however, varied considerably in age, as certain parts of it were of much more recent development than others. The fibrous tissue strands were not, as a rule, sharply defined, but extended irregularly among the lung tissue. The older portions were fairly vascular, and the capillaries were well formed as a rule. Many of these capillaries were surrounded by an extensive zone of lymphocyte aggregation, and in fairly frequent places inflammatory endarteritic processes, and even complete vascular obliteration, could be seen (Fig. 11). Remnants of included alveoli were common in the fibrous tissue, and they appeared as irregular, elongated,

duct-like acini, or merely as a small collection of darkly staining, small, somewhat cubical-shaped cells (Fig. 12). In the older portions of fibrous tissue there was a considerable representation of elastic tissue, existing in fine wavy threads. In the more recent parts the normal elastic tissue elements had apparently been more or less destroyed. At the margins of these fibrous trabeculæ the lung tissue for some distance outward showed a condition of organizing pneumonia (Fig. 13). This organization had occurred in much the same way as in the cases of organizing following acute pneumonia. Evidently in these places the inflammatory process had

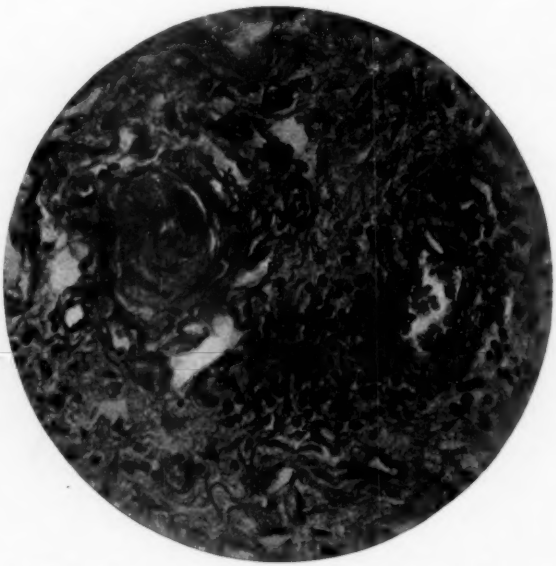

FIG. 11.—Syphilis of lung. Section from a fibroid area, showing one vessel surrounded by lymphocytes and another almost completely obliterated by endarteritis. × 300.

not led to destruction of the lung structure, and the inflammatory exudate into the alveoli was being removed and replaced by the process of organization. In some places this organizing process was more extensive and more confluent, as some of the air spaces evidently had in parts been destroyed. The acute pneumonic areas seen grossly were in a state of gray hepatization, and they included numerous small foci of abscess formation. In no part of the lung, and after repeated search in a large number of situations, could either tubercle bacilli or spirochetes be discovered. Pneumococci and some staphylococci were commonly present in the gray hepatization areas.

The bronchial glands were slightly enlarged and pigmented, but showed no fibrous or tuberculous change. The bronchi were considerably congested, and their mucosa atrophied from chronic bronchitis. The larynx and epiglottis presented no abnormality except some congestion, and there was no smooth atrophy of the base of the tongue. Indeed, the papillæ at the base of the tongue were slightly hypertrophied.

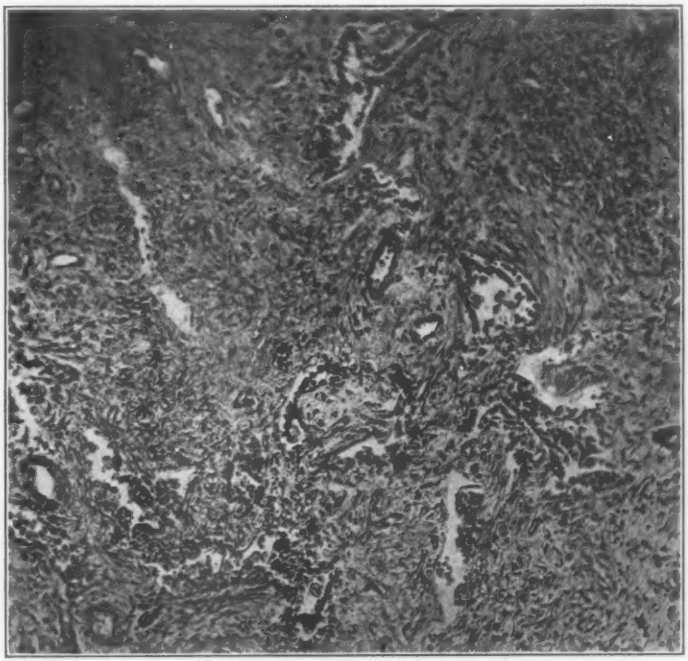

FIG. 12—Syphilis of lung. Dense fibrous area, including remnants of excluded partly destroyed air alveoli. × 140.

The pericardial sac contained about six ounces of a clear, blood-stained fluid. There were a few old adhesions at the base, around the origin of the great vessels, and the entire surface of the pericardium was covered by a shaggy fibrinous exudate. No organisms, tuberculous or otherwise, were found in this exudate, and considering the possibility of this inflammation being syphilitic, spirochetes were searched for, but could not be demonstrated. It appeared to be one of those cases of pericarditis which are found fairly frequently in association with nephritis.

The heart (550 grams) showed no special change beyond dilatation and some hypertrophy of the myocardium of both ventricles,

particularly the left. The aortic valves, the aorta, and coronary arteries, were only moderately atheromatous. The kidneys presented the usual appearances of advanced chronic nephritis. The liver (1500 grams) showed a deep typically syphilitic scar on its anterior upper surface, and microscopically it was found that the portal space fibrous tissues were considerably thickened, and contained dense aggregations of lymphocytes. No endarteritis, however, could be determined in the hepatic vessels.

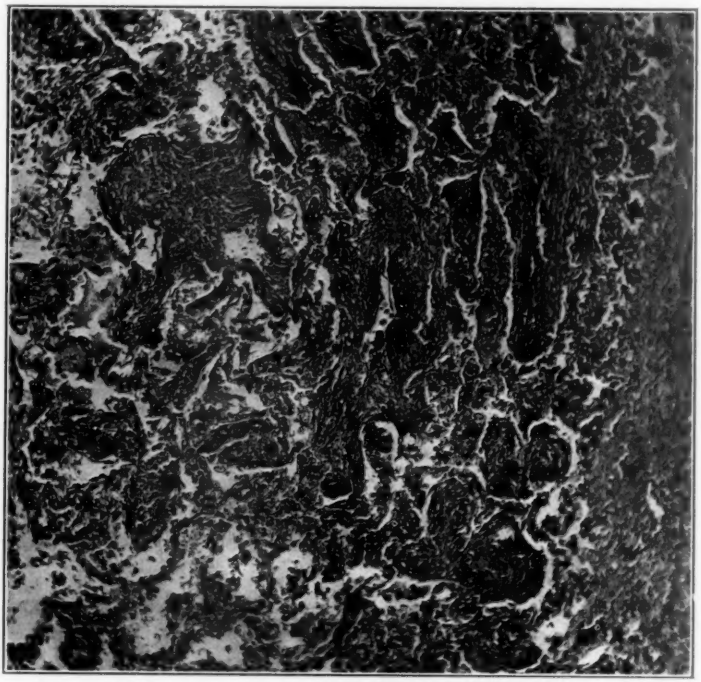

FIG. 13.—Syphilis of lung. Organization of the inflammatory contents of air alveoli. × 110.

The intestines showed no particular change, except the rectum which was stenosed by a ring of dense fibrous tissue about two inches above the anus. There was no ulceration around the constriction, and no glandular enlargement in relation to it. Microscopically, it was composed of dense fibrous tissue, and contained no evidences of tuberculosis. The mesenteric glands were not specially enlarged.

The meninges of the brain at the vertex were slightly thickened, and in patches adherent. The vessels at the base were extensively atheromatous, and there was considerable atrophy of the frontal

convolutions, as in early general paralysis. The interior of the brain only showed extreme edema without any gross lesion.

The spinal cord showed the usual degeneration of the posterior columns characteristic of tabes dorsalis.

These two cases then are examples of one of the varieties of syphilitic involvement of the lung.

Case I occurred in a subject who presented no other manifestations of syphilis in any other situation, and the pulmonary fibrosis was evidently of a very chronic, completely healed type. In the second case the process was much more recent, more widespread, and its relation to syphilis more definite from the numerous coexisting syphilitic lesions, as well as the suggestive vascular and other peculiarities in the fibrous tissue overgrowth in the lungs themselves. Both cases also conformed to the type generally described as diffuse interstitial syphilitic fibrosis as distinguished from the gummatous variety and the white pneumonia which is particularly found in congenital syphilis.

Diffuse syphilitic fibrosis has been considered by Pancritius to extend outward from the hilus, and Goodhart[44] advocated an extension from the pleura. In Greenfield's case, however, the pleura was free. Heller believed it to be a proliferation of the interlobular and interalveolar connective tissue, and partly from the vessel adventitia and Storch considered the process of diffuse syphilitic fibrosis to be originally derived from isolated areas which, through thickening and consequent lymphangitis, spread and united into a diffuse induration. In Case I the indurative process had evidently already become chronic and quiescent, but in Case II the process was comparatively recent, and still more or less active. The effects produced seemed to be consequent on a destruction of lung tissue, the damaged, irritated, and inflammed areas becoming organized by scar tissue, and the appearances presented depending on the severity, duration, and extent of the destructive process.

In one of the cases there was some resemblance in places to organizing pneumonia as well as the superimposed complication of an ordinary terminal pneumonia, and in this connection it is rather interesting to note that many of the older authors, such as Pavlinoff,[45] Kopp,[46] Sokolowski,[47] etc., have described a condition of syphilitic bronchopneumonia. Virchow guardedly admitted the possibility, but was doubtful of any special characteristics, and Ruhemann[48] stated that in acquired syphilis, bronchopneumonia was not so definite an event as in the congenital cases, and if such a thing existed it could not be distinguished from any other bronchopneumonia. Orth[49] and Birch-Hirschfeld[50] held that any relationship between bronchopneumonia and syphilis was very doubtful, and it does not now enter into any modern classification of the varieties of pulmonary syphilis. Pneumonia, although not of the type mentioned in the older writings, and although generally very

localized and irregular, is, however, a condition to be considered in pulmonary syphilis, as before fibrosis can occur some irritation or destruction must exist with the resulting production of a pneumonic process.

The conception of "syphilitic phthisis," as described in the older writings, has also undergone a similar modification. The condition known then as "phthisis ex lue venerea" appeared to be relatively common, and even Virchow agreed that cavities might form to produce a syphilitic phthisis. As late as 1881 Pancritius[51] described "syphilitic phthisis" as one of the most frequent of all diseases, his conclusions, however, being based almost exclusively on clinical data. Sokolowsky (1883) also described this condition, but Hiller[52] (1884) denied absolutely any such process, and following the discovery of the etiology of tuberculosis, practically all the cases previously described as syphilitic phthisis have become recognized as obviously tuberculous. The lack of proper distinction between syphilitic and tuberculous affections of the lung still gives rise to some difficulty, but in the older works provided some of the most surprising clinical pictures. Stengel[53] quotes Brambilla's case of a supposedly tuberculous patient who was given the mercurial inunction intended for a syphilitic in the adjacent bed, and this was followed by the prompt recovery of his symptoms. Gummatous masses may occasionally break down and form small cavities, but the majority of such cavities as do exist in syphilitic lungs are undoubtedly bronchiectatic. Tripier and also Bériel,[54] although probably somewhat too emphatic, relate the majority of cases of bronchiectasis to a syphilitic basis.

Clinically, the distinction between syphilis and tubercle is frequently difficult. In the works of Senger[55] and Porter,[56] Schnitzler,[57] Schiffmacher,[58] Schech,[59] Zinn,[60] and others numerous points of distinction have been advocated. The sputum examination, the temperature, and the presence of other syphilitic lesions may be of some little help, but the location and character of the signs by physical examination is perhaps of more importance. Pancritius, from a study of 106 cases, and Grandidier,[61] from 20 cases, came to the conclusion that the chief differential diagnostic point lay in the predominating affection of the middle lobe of the right lung in syphilitic processes, and Cube,[62] Kaposi,[63] and Aufrecht,[64] and many others have concurred in this. Ruhemann in 90 cases found 52.2 per cent. in the right lung alone, 11.1 per cent. in the left lung alone, 36.7 per cent. in both lungs. The right middle lobe was affected in 42.2 per cent., upper lobes 20 per cent. (both 9.8 per cent., right 7.7 per cent., left 3 per cent.), both lower lobes 8.8 per cent.

These data, however, refer to all kinds of pulmonary syphilis. White pneumonia, from most descriptions, is most commonly in the upper lobes or in the right middle lobe, and diffuse interstitial

fibrosis is generally met with in the lower lobes. Although the preponderance of tuberculous affections of the lungs are centred in in the upper lobes, yet, as they are commonly found in all situations in the lung, the diagnosis by location between syphilis and tubercle is thus necessarily very uncertain.

Pathologically even there may be uncertainties of distinction, as was noted by Saalfeld,[65] Ramdohr,[66] etc., between syphilis and tubercle, and Herxheimer (1907) observed that in some few cases the two processes were quite indistinguishable. As a rule, however, tuberculous conditions leave some definite characteristic traces both in gross and microscopic examination. The presence of giant cells is no absolute criterion of tubercle, as they have also been noted in syphilitic processes, particularly in relation to gummas, by Baumgarten,[67] Brodowsky,[68] Hansemann,[69] Brandenberg, etc. The finding of tubercle bacilli is of course positive of tuberculosis, yet if not discoverable it does not contraindicate tubercle, as the organisms are often particularly hard to demonstrate in many chronic, definitely tuberculous lesions. The demonstration of spirochetes has about the same relationship to syphilis, as they are only rarely found. Levaditi, Roche, Brandenburg and others have observed this, and also stated that in all the more chronic lesions of acquired syphilis they are relatively infrequently found. In the manifestations of congenital syphilis, however, they are, as a rule, much more frequently demonstrable. In neither of the two syphilitic cases detailed in this present communication could either spirochetes or tubercle bacilli be observed in any situation.

As indicative of syphilitic lesions in the lung, the peculiar hyaline appearance of the connective tissue, the finding of gummas if present, the high degree of vascularization as compared with tuberculous processes, the perivascular lymphocyte aggregations (Fig. 11), and particularly the endovascular changes (Fig. 11), are important. These vascular changes have been observed, as in syphilitic conditions in other organs, in the lung by Birch-Hirschfeld, Greenfield,[70] Petersen,[71] Pavlinoff, Councilman,[72] Storch,[73] Brandenburg, etc. It has been suggested that the whole process of fibrosis depends on this vascular obstruction, but in considering the relatively small number of vessels involved this cannot be so.

There still remain to be considered those cases where tubercle and syphilis coexist. Rindfleisch (1894) described a case of mixed tuberculosis and syphilis. The subject was first tuberculous, and syphilis was subsequently acquired. After death both processes were distinct in the lung, the syphilitic nodules being encapsulated from the tuberculous foci. Borst[74] has referred to a combination of miliary tuberculosis, with syphilitic affections, the syphilitic process encapsulating the tubercles. Hansemann[75] takes the stand that most syphilitic conditions on the lung are apt to become secondly infected by tuberculosis. Out of 22 cases which he examined, in

only 5 were tuberculous lesions not demonstrable. Eppinger[76] and Potain[77] came to somewhat the same conclusion, but Flockmann and also Mauriac[78] have denied any more than an accidental association. Keyes[79] also has observed that the combination of syphilis and tubercle has been much overrated. Fournier[80] has stated that when syphilis was engrafted on a proved case of tuberculosis the course of the latter became more rapid and severe. Also when pulmonary tuberculosis became evident in the early stages of lues, there was a rapid extension of the tuberculous process, and the prognosis was very grave. When tuberculosis, however, was consequent to an old standing luetic infection the disease was apt to assume the form of a tardy sluggish afebrile type.

As far as these cases would seem to show, organizing pneumonia is a condition which generally can be fairly easily distinguished from a syphilitic process. There are not the same vascular changes, nor is there the same tendency to destruction, and the irregularity of the whole process in syphilis is also strikingly different.

Such conclusions as may be drawn from these 10 cases of chronic pneumonia are:

1. That they are a possible sequence of acute pneumonia.

2. That they are particularly found in subjects debilitated by some intercurrent condition, but that no single factor such as cardiac conditions, nephritis, arteriosclerosis, alcoholism, tuberculosis, or syphilis is responsible for its production.

3. The onset is extremely irregular in type, and may be acutely febrile, simulating the usual commencement of a croupous pneumonia in subjects of the same age (Cases IV, VII, IX, and X), or typical signs of pneumonic consolidation may be evident without there having been any especial initial pneumonic symptoms (Cases II, III, V, and VI), or there may even be no increase in temperature or abnormality of the pulse and respiration rates (Cases I and VIII).

4. The prognosis in such conditions is bad, as not only is death very frequent from cardiac insufficiency, but complications, such as empyema, pericarditis, peritonitis, meningitis, etc., are extremely frequent, and what is very important that any of these conditions may supervene even after long periods of apparent quiescence of the pneumonia—7 out of the 10 cases were complicated in this way, an infinitely higher proportion than occurred in the rest of the pneumonia series; 41 out of 95 cases of lobar pneumonia, including 9 which had become organized, and 10 out of 64 cases of bronchopneumonia, including 1 which was organized, were complicated.

5. Such conditions may undoubtedly be recovered from as far as symptoms are concerned, yet maintaining physical signs of pneumonic consolidation. It is just such cases which are apt to be mistaken for tuberculosis or possibly syphilitic fibrosis. In this

connection it is also possible that the development of bronchiectasis or subsequent tuberculous infection may further complicate the case.

6. Collapse, tubercle, infarcation, and syphilis of the lung, etc., are distinguishable from chronic pneumonia.

7. Once organization processes in the lung have advanced to any marked extent one cannot imagine any complete restoration, as some cicatrization must be permanent.

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# REVIEWS

DIFFERENTIAL DIAGNOSIS. By RICHARD C. CABOT, M.D., Assistant Professor of Clinical Medicine, Harvard University Medical School, Boston. Pp. 753; 195 illustrations. Philadelphia and London: W. B. Saunders Company, 1911.

IT is not to be denied that Dr. Cabot, more than anyone else in the United States, has been instrumental in devising new and improving old methods of teaching medicine. His latest book on differential diagnosis indicates no diminution of his originality, and whatever may be the opinions of his readers, and doubtless they will vary a good deal, no one can read it without being stimulated and aroused to perfect himself in the fundamental and most difficult department of medicine, diagnosis. Like all things, however, this book is not wholly new, but its evolution can be traced through a series of other works of greater or less importance. I do not mean to imply that Dr. Cabot has consciously copied. It is more than likely that he is not personally familiar with many of the books in which a somewhat similar attempt has been made, but these books, at least those of them that are really good, have influenced medical thought and medical literature, and it is altogether likely that without them Cabot's book would not have been possible. A pattern of such work was Richard Bright's *Reports of Medical Cases*. Although it is not strictly a work on differential diagnosis, nevertheless both Bright's and Cabot's books are constructed on essentially similar lines. Bright, it is true, groups his cases sometimes according to a morbid lesion, rather than according to subjective and objective symptoms. Hilton's work on *Rest and Pain* incidentally discusses a good deal of differential diagnosis, particularly in reference to subjective symptoms, and has also played its unconscious part. Another book now wholly forgotten is a work on *Practical Medicine*, edited by John M. Galt, published in 1843, in which the subject of medicine, classified largely according to important symptoms, is wholly illustrated by actual cases. Still another to which reference should be made is Pershing's *Diagnosis of Nervous and Mental Diseases*, in which the classification is wholly according to symptoms, an ambitious and reasonably successful attempt.

Dr. Cabot's book consists of a small amount of comment and 383 histories. These are all presented under four heads: (1) The history, clinical symptoms, physical signs, and laboratory reports;

(2) the discussion which involves more or less differential diagnosis; (3) the outcome; and (4) the final diagnosis. In addition, there are diagrams at the beginning of each chapter to show graphically the relative frequency of the various causes of the symptom under discussion. These diagrams are based partly on Dr. Cabot's own investigations, partly upon statistics obtained from the literature. There is also at the end of many of the articles a table of differential diagnosis. It is upon the case histories that the value of the work will ultimately depend. These are presented with the dogmatism so characteristic of Dr. Cabot and in language that not infrequently is unconventional, but which is always precise.

There will be many instances where the reader will disagree with Dr. Cabot, but this only adds to the interest of the book. Often Dr. Cabot states that a differential diagnosis between certain things is impossible, and fails to mention physical signs which might aid the differentiation. He is fond of speaking of wild and untamed physical signs, which, according to him, are signs absolutely in disagreement with the diagnosis, and therefore serve to indicate how carefully the case has been studied. I think that few will be willing to accept dynamic aorta as a final diagnosis. The important thing is that Dr. Cabot has produced a book on unconventional lines that is useful, and, more than its mere utility, is stimulating.

Regarding the diagrams, we cannot share his enthusiasm. Undoubtedly it is desirable to have numerical statements of clinical facts and such statements are of importance if they are true. The presentation of these diagrams, even if they are inaccurate, may serve to call attention to the necessity of gathering further statistics, and they are at least no worse than the hazy ideas upon the subject possessed by some of us. However, it is my impression that should this further study be undertaken, the appearance of some of the diagrams will be very radically changed. J. S.

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PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics in the Jefferson Medical College, Philadelphia. Volume I, pp. 355; 18 illustrations. Volume II, pp. 397; 51 illustrations. Philadelphia and New York: Lea & Febiger, 1911.

VOLUME I of *Progressive Medicine* begins with a discussion of the surgery of the head, neck, and thorax, by Charles H. Frazier.

After devoting 12 pages to the surgery of the face, jaw, mouth, and tongue, he deals with the neck, especial attention being given to tuberculous adenitis. Next follows a full account of various conditions of the thyroid, thymus, and parathyroid glands. The succeeding 28 pages are given over to a consideration of the surgery of the brain, especially tumors, and the cranial nerves, the latter being considered in great detail. In a like number of pages devoted to thoracic surgery, the more important recent advances dealing with the heart, lungs, pleura, and esophagus are taken up, together with a concluding section on the mammary gland. In an article of 132 pages, John Rurāh has furnished an excellent and complete summary of the work done during the last year in infectious diseases. After paying a graceful tribute to the memory of Robert Koch, he calls attention to the most notable therapeutic achievement of the year, the introduction of salvarsan by Ehrlich and Hata. A discussion of various general factors in the spread and production of disease is followed by a consideration of most of the infectious diseases, including those due to parasitic agents. Cholera receives full and timely recognition. Poliomyelitis, tuberculosis, and typhoid fever are accorded most thorough treatment. Floyd M. Crandall, in 31 pages, deals with certain phases of diseases of children. Infant mortality, hemorrhagic disease of the newborn, diseases of the urinary tract, are among the subjects discussed. In addition, 19 pages are devoted to the question of infant feeding and the stools and digestion in infancy. Dr. D. Braden Kyle's interesting contribution on Rhinology and Laryngology occupies 43 pages of the volume. He takes up important advances in our knowledge of the nose and the accessory sinus, the pharynx, larynx, and the tonsils. In the concluding 25 pages on otology, Arthur B. Duel discusses at some length deaf mutism, otitic meningitis, the Eustachian tube, sigmoid sinus thrombosis, the value of the Wassermann test in internal ear disease, and the use of vaccine therapy for purulent aural infections. As during each succeeding year the volumes of *Progressive Medicine* appear, the value of the work as a reliable guide to medical and surgical progress becomes more and more apparent. In this respect the first volume of 1911 is no exception to the many that have preceded it.

Two thirds of Volume II of *Progressive Medicine* deals with topics that are largely surgical. In the first 40 pages William B. Coley goes at length into the subject of hernia. The operative treatment, numerous unusual forms of hernia, and various complications of the condition are taken up. Arpad G. Gerster has furnished an admirable review of 96 pages on the surgery of the abdomen. He enters into the many important advances in abdominal diagnosis that have of late resulted from the use of Röntgen rays, and describes, among other interesting procedures, the use of Momburg's aortic tourniquet and a method

of draining ascites into the subcutaneous abdominal tissues. The omentum and stomach are considered; under the latter especial attention is paid to the surgery of gastroptosis, acute gastric dilatation, hemorrhage, and ulcer. A number of pages devoted to the intestines and appendix conclude his observations on the intestinal tract proper. Finally, he considers the liver and portal veins, the pancreas, and spleen. Under the latter heading, Banti's disease is fully discussed. It is of interest to note that the recent articles on the Cammidge reaction are unanimous in regarding the test as useless for the diagnosis of pancreatitis. The gynecological section of 104 pages, by John G. Clark, comprises 33 pages on the cancer problem in general and that of the uterus in particular. The remaining pages contain an excellent digest of a number of subjects of live interest, among which may be mentioned uterine fibroids, displacements and prolapse of the uterus, pelvic inflammatory diseases, the relationship between rectal and pelvic diseases, backache, and various phases of the menopause. The medical portion of the volume consists of Alfred Stengel's usual valuable contribution, which occupies 101 pages. Under the blood, he has entered fully into pernicious anemia, chlorosis, the leukemias and chloroma, hemophilia, purpura, and Addison's disease. Then follow discussions of myxedema and cretinism, Banti's disease, and splenomegaly. Several pages suffice for a review of what has been done of late on Hodgkin's disease and diabetes insipidus, whereas diabetes mellitus and exophthalmic goitre embrace the concluding third of his article. The final section of the volume contains 25 pages by Edward Jackson on ophthalmology. Before he takes up diseases of the several portions of the eye, as the conjunctiva, cornea, uveal tract, crystalline lens, retina, optic nerve, and lacrymal apparatus, he calls attention to the influence of salvarsan on the eye, and concludes by considering injuries to the eye. The entire volume is of exceptional interest, and its perusal will amply repay all who desire to familiarize themselves with the many important advances that have recently occurred in the branches of medicine and surgery which it covers. G. M. P.

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DIAGNOSTIK DER NERVENKRANKHEITEN. DR. L. E. BREGMAN, Oberarzt am städtischen jüdischen Krankenhaus in Warschau. Mit einem Geleitwort von HOFRAT PROF. DR. H. OBERSTEINER in Wien. Pp. 535; 193 illustrations. Berlin: S. Karger, 1911.

THIS is essentially a diagnosis for diseases of the nervous system. The plan of the work is excellent, but its uses will be limited because the work is not sufficiently extensive. Its plan is to present symptoms

and to mention all the possible diseases in which a given symptom may be present. For example, when discussing motor symptoms, those relative to the peripheral and cranial nerves are discussed, and then those relative to cerebral and spinal diseases, but there is no distinctive effort to cover the symptoms of any one disease unless it comes purely within the classification of motor, sensory, or special symptomatology. For example, while locomotor ataxia is considered in several places, the disease as a whole is not taken up, but when discussing aphasia the subject is comprehensively handled because it is considered as a distinct symptom. While this method has its advantages, its disadvantages are apparent.

From the standpoint of symptomatology it is perhaps the best presentation that the reviewer knows, for no symptoms has been neglected. The extent of the subject is comprehensive and neurologists will find most symptoms amply discussed, although by no means exhaustively.

It has the usual failing of most foreign text-books, articles, and monographs, that is, references to American authors are sadly lacking. Why this should be so in the present age of scientific medicine, especially considering the advances which have been made by American physicians, is difficult to understand. There is probably only one Continental neurologist who consistently mentions Americans—Oppenheim—and it is indeed with pleasure that American neurologists contemplate that he is probably the best that Europe has. Therefore, there is less reason for others to be provincial. However, the foreigner is not altogether at fault, for it is a notorious fact that American authors, not always neurologists, have a predilection for mentioning foreign authors and neglecting their own countrymen. This is not only true in scientific articles, but is also true in the abstract department of some American journals, for while the presumption is that a German journal, for example, is for the Germans, and then for others, a French journal for the French, and then for others, an American journal (supported by Americans) is first for the others, and then for Americans. This is only too true.

Specifically, it is difficult to criticise this book, and only certain subjects will be touched upon. The description of nerve palsies is excellent, but it is interesting to note that the author refers only in a footnote to the newer classification of deep, epicritic, and protophathic sensibility. In discussing the disturbance of sensation resulting from cortical lesions, he fails to refer to segmental disturbances, but this would be expected, inasmuch as Americans first called attention to it. In discussing the occurrence of the Babinski reflex in motor cortical lesions, he states that it is absent in many cases; but it has recently been pointed out, however, that this phenomenon is present only in cortical lesions limited to the leg centre. In discussing aphasia, he disposes of Marie's newer

ideas almost in a paragraph, and sticks to the older classifications. These, however, are only minor criticisms. The illustrations are fairly good, although it is difficult to understand why in most German books, whenever the author has an original picture, the words "Eigene Beobachtung" are always given in the legend, for the presumption is that if not otherwise indicated, the pictures are by the author. T. H. W.

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PRACTICAL TREATMENT. A HANDBOOK OF PRACTICAL TREATMENT. In three volumes. Edited by JOHN H. MUSSER, M.D., Professor of Clinical Medicine, University of Pennsylvania, and A. O. J. KELLY, M.D., Assistant Professor of Medicine, University of Pennsylvania. Volume I; pp. 909; 227 illustrations. Philadelphia and London: W. B. Saunders Company, 1911.

"THERE is in Medicine an art and a science, each mutually dependent on the other. The practising physician's chief concern, however, is with the art, rather than the science. . . ." With this as the opening sentence, the editors strike the keynote of the work before us. This expression, coming from the diagnostician, the consultant, the teacher, the laboratory expert, and the practising physician, each of whom is represented in one or the other or both of the two editors of this treatise, has an authoritative significance of considerable interest. Especially is this true to-day when the mutual dependence of the art and the science is coming to be recognized by the more thoughtful of those governing the direction of medical development.

The time is ripe for just such a book as this. The treatment of many diseases has, through experiment, passed either entirely out of empyricism, or theory and reasoning has led scientists far toward the solution of the body's defensive and offensive mechanism. *A Handbook of Practical Treatment*, therefore, written today by such international authorities as compose the list of 79 contributors to this work, constitutes an indispensable aid to the practitioner.

Among the contributors are surgeons and specialists in various branches of medicine. This is, as the editors rightly term it, an "innovation" by which "the treatment of certain borderland and other diseases" is discussed by "physician and surgeon" or specialist "so that the reader may have the benefit of the points of view of both."

The book is in marked contrast to former works on this subject, in that drugs and prescriptions constitute a very minor part.

Among comparatively new subjects in a work of this kind are the following: Preventive Treatment; General Principles of Dietetics, Serum Therapy, and Organotherapy; The Rest Cure, The Work Cure, and Psychotherapy; Exercise; Massage and Mechanotherapy;

Hydrotherpay and Balneotherapy; Climatotherapy and Health Resorts; Artificial Aërotherapy; Electrotherapy and Radiotherapy.

"Preventive Treatment" deals with National, State, and Municipal Health Boards. Under this head also appears "Prophylaxis of Infectious Disease," "Disinfection," and "Protective Inoculation," the latter being but briefly treated, as it is more fully dealt with under serum therapy.

To the subjects "General Principles of Dietetics" and "Dietetics of Infancy" is allotted 118 pages in this volume of 909 pages. Technical discussions of these subjects are omitted, but sufficiently detailed consideration of methods of determining food values for infant and adult is given to enable the practitioner to exercise his own judgment in making up dietaries. This is to be preferred to the usual custom of itemized meals for pathological conditions, often wholly unsuited to the patient in question.

The chapter on "General Principles of Serum Therapy" will be read with much interest. It is a thoroughly up-to-date authoritative discussion of this foremost subject in modern medicine. Protective and curative inoculations in certain disease conditions are considered. Possibly lack of space prevented, but it would have been helpful to the practitioner had a few temperature charts been introduced to show some of the reactions and their significance.

In the chapter on "Organotherapy" the writer takes a very gratifyingly conservative view of the subject which it is to be hoped will check the irrational therapeutist and medical faddist. The chapter on "Exercise, Massage, and Mechanotherapy" is probably the most comprehensive treatment of the subject that has as yet appeared—certainly in a handbook.

Hydrotherapy and Balneotherapy, recognized as essential to most modern hospitals, are thoroughly discussed and illustrated under this head.

The subject of Climatotherapy, usually briefly dealt with in text-books and too extensively treated of in special publications, is presented succinctly, with, however, specific reference to resorts and their suitability to different pathological conditions.

While, as already stated, the consideration of drugs, as such, receives little space in this volume, the subject of drug action is dealt with under the headings "The General Principles of Drug Treatment" and "Drug Poisoning and Drug Habit."

The index, a portion of these large works often recklessly neglected, is practical, thorough, and, so far as tested, accurate.

The book is possibly too bulky, and this is only the first volume. When, however, one considers the immense amount of material which may be comprised under the term "Treatment," the editors, by judicious omission, will be found to have done well in reducing the mass to even 909 pages. Long dissertations on drugs whose actions are imperfectly understood and on methods of doubtful merit are conspicuously absent.

As one reads, in review, the chapters which compose this volume, the impression is that here are the modern methods acceptable to authoritative and conservative medical men. Such a book must, therefore, be an essential in the equipment of the practising physician who would guard himself against the fallacies and errors which have brought treatment into such disrepute from time to time.

Lack of space prevents detailing further the many features of this work which deserve notice. One cannot, however, close this review without a word regarding Dr. A. O. J. Kelly, whose death has proved such a loss to American medicine. Conversant with the laboratory as well as the clinical side of medicine, he was eminently fitted to act, together with Professor John H. Musser, as the "guiding hand" in the production of this valuable addition to medical literature.

C. N. B. C.

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SEHPROBENTAFELN ZUR BESTIMMUNG DER SEHSCHÄRFE FÜR DIE FERNE. FÜR DIE ZWECKE DER PRAXIS UND MIT BESONDER BERÜCKSICHTIGUNG DER BEDÜRFNISSE DER ÄRZTLICHEN GUTACHTERTÄTIGKEIT. TEST OBJECTS FOR DETERMINING THE VISUAL ACUITY FOR DISTANCE. INTENDED FOR PRACTICE AND WITH PARTICULAR CONSIDERATION OF THE REQUIREMENTS OF MEDICAL CERTIFICATION. By DR. V. AMMON, Army Surgeon and Oculist in Munich. Second edition: 8 lithographic tables. Munich: J. F. Lehmann, 1909.

THE purpose of the designer of these test cards has been not simply to offer to the examiner test types and objects which might be in some respects an improvement upon the many existing ones, but his object has been to supply a method of testing central vision which shall be as far as possible objective in character and to permit ready comparison between and control of the statements of the person under examination by suitable variation of the methods of examination. Direct view of the test object, controlled by reflection of the same in a mirror, is one of the ingenious devices employed as follows: The subject is asked to read the lowest line he can decipher. He is then requested to read from an identical card (in reverse type) when reflected in a mirror. If the two agree the result may be accepted as the real degree of central vision. A simulator would be liable to select the same lines in each test, not knowing that the reflected letters can be so arranged that their virtual distance is greater than by the direct test, and thus require a higher degree of visual acuity. The cards also contain a number of other ingenious devices which fulfil a needed requirement not to be found in the usual armamentarium of the oculist.

T. B. S.

# PROGRESS

OF

# MEDICAL SCIENCE

## MEDICINE

UNDER THE CHARGE OF

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**The Etiology of Scarlet Fever.**—S. BERNHARDT (*Deutsch. med. Woch.*, 1911, xxxvii, 1062) referred in his first report to cell inclusions in scarlatina. The present note deals with these bodies. He found certain cellular inclusions resembling the trachoma bodies in the mesenteric lymph glands of three patients dying early in the course of scarlet fever and in the kidney cells of one case. Similar inclusions have been found in the lymph glands of apes infected with scarlet fever. On injecting these glands into other apes, a disease like scarlatina in man was produced. In the control material examined, such inclusions have not been found. P. A. HOEFER (*Ibid.*, 1911, xxxvii, 1063) also reports the finding of intracellular bodies in scarlatina. The bodies he describes are larger and differ from those of Bernhardt. Prof. Hartmann, who has seen the preparations of both Bernhardt and Hoefer, expresses the opinion that the findings of these two workers are not identical, but considers it possible that each may represent stages in the development of a parasite. Hoefer's inclusions were found in the cells of the spleen, lymph glands, and mucous membranes of fatal cases of scarlatina.

**A Modification of the Acetic Acid Test for Albumin in the Urine.**—GLAESGEN (*Münch. med. Woch.*, 1911, lviii, 1123) calls attention to a method of employing the acetic acid test for the detection of albumin which has been used for years in France. Method: 20 c.c. of urine, about three-fourths of a test-tube 1.5 cm. in diameter, are treated with five drops of 20 per cent. acetic acid, mixed, and one-half poured into a second test-tube. The contents of one tube are boiled, the other

serving as a control. Albumin produces a cloud or precipitate in the boiled tube. Before testing, the urine must, of course, be perfectly clear; if necessary, shake it with Kieselguhr and filter. If the acetic acid causes a cloud in the cold (nucleo-albumin), it is cleared by filtration before boiling. With an alkaline urine, acidulate slightly to prevent the precipitation of the phosphates, or, if a precipitate of phosphates appears when the urine has been treated with acetic acid and boiled, a few more drops of the dilute (20 per cent.) acid may be added to dissolve it. This will not redissolve even a slight albuminous cloud, provided the urine is not boiled again. Glaesgen has compared the test performed in this way (1) with the usual method, *i. e.*, boiling the urine and then adding dilute acetic acid; (2) with the acetic acid and potassium ferrocyanide test; and (3) with Heller's test. He used urines with known albumin content and diluted them with urine which was negative to Spiegler's reagent. He found that the test as described would detect albumin in a dilution of about 1 to 180,000, the heat and acetic acid test in 1 to 130,000, acetic acid and potassium ferrocyanide, 1 to 70,000 after standing some time, and Heller's 1 to 35,000. In no case where physical examination of the patient did not reveal an adequate cause for a trace of albumin was the test positive. He therefore thinks it does not react to the minute quantity of albumin present in normal urine. When a patient is on a milk diet, the urine may be so poor in salts that a trace of albumin may be missed with this test. But the addition of sodium chloride obviates this difficulty.

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**Salvarsan Milk.**—Jesionek (*Münch. med. Woch.*, 1911, lviii, 1169) has observed cases similar to those of Taege, Duhot, and others, in which the suckling infant of a syphilitic mother was apparently cured of lues following the administration of salvarsan to the mother. Unlike previous observers, however, Jesionek has demonstrated arsenic in the milk of the syphilitic mother after treatment with salvarsan. He believes the benefit to the infant may be due quite as much to the arsenic as to the antibodies in the milk. Furthermore, there is the possibility that the milk may contain endotoxins. To eliminate antibodies and endotoxins, the author injected salvarsan intravenously into a goat and used the milk, which, however, did not yield an arsenic mirror, as food for a child of five years suffering with acquired lues. There were marked lesions of the skin and mucosæ, including condylomata. The child received no other treatment. There was a rapid and complete symptomatic cure coincident with the taking of the milk.

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**A Blood Counter for Leukocytes and Cytodiagnosis.**—R. Dunger (*Münch. med. Woch.*, 1911, lviii, 1131) has enlarged the ruled area of the hemocytometer so that it covers forty-nine instead of nine square millimeters. He used the Türck ruling. The chief advantage of the counter is in cases with marked leukopenia and in the cytodiagnosis of serous fluids, especially cerebrospinal fluids, in which the cells are few in number. The apparatus is made by Zeiss.

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**On New Characteristics of the Urine in Health and Disease.**—H. Pribram (*Deutsch. Arch. f. klin. Med.*, Leipzig, 1911, cii, 457) has made interesting observations, injecting various portions of normal and

pathological urines into rabbits and noting the effects. He finds (1) that the injection of urine gives rise to the formation of hemolysins, precipitins, and complement binding antibodies in the serum of the injected animal. The precipitin formation is always more marked with the injection of normal urines than with albuminous; the fixation of complement, on the other hand, is greater when one uses albuminous urines for injecting the experimental animals. (2) The injection of urinary sediment and of the alcohol-ether insoluble portion of the non-dialyzable fraction ("lysogenous substance") of the urine produce the same changes in the serum of the injected animal as described under (1). (3) The "lysogenous substance" contains the normal urinary albumin and a number of other substances. In chronic nephritis this fraction is practically normal, whereas in acute nephritis its increase runs parallel to the amount of albumin. (4) Both qualitative and quantitative examination of this fraction show that its chief constituents are not albuminous. (5) The substances in the urine which act as antigen probably arise in the renal cells. (6) The urine is markedly toxic. The same is true of the lysogenous substance and of the sediment. Repeated injections seem to raise the resistance of the animal to the poisoning. (7) The symptoms of uremia are possibly due to a retention of the toxic bodies contained in the lysogenous substance. (8) The "Mörner fraction" of the urine contains traces of lysogenous bodies, but no precipitin or complement binding antigens, and is not toxic to animals. In the examination of the urine of 50 patients with hypertension, the usual heat and acetic acid test showed a trace of albumin in 15, the acetic acid and heat in 36 cases. In other conditions with a trace of albumin similar results were secured with the two methods of employing acetic acid.

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**The Acetonitryle Reaction in Basedow's Disease.**—G. Ghedini (*Wien. klin. Woch.*, 1911, xxiv, 736) has made an experimental and clinical study of the acetonitryle reaction of Reid Hunt. The latter found that the feeding of thyroid to white mice greatly increased their resistance to the poisonous effects of acetonitryle. Ghedini has used the blood of patients with a variety of diseases as food for mice. It is of interest that in three well-marked cases of Basedow's disease the reaction was strongly positive, whereas in two doubtful cases (formes frustes) the resistance of the mice remained unchanged.

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**The Wassermann Reaction in Lead Poisoning.**—A. Dreyer (*Deut. med. Woch.*, 1911, xxxvii, 786) has examined sera from a number of cases of lead poisoning. Of 35 cases of plumbism, 4 gave a positive Wassermann reaction; 25 were tested according to Stern's modification of the Wassermann technique, and of these, 12 were positive. The positive cases gave no history of syphilitic infection nor could signs of lues be found on physical examination. The author believes the positive reactions were due to the lead poisoning *per se* and not to a latent lues.

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**A Urinary Reaction in Progressive Paralysis.**—H. M. Stucken (*Münch. med. Woch.*, 1911, lviii, 855) has repeated the work of Butenko, who found that the urine of patients suffering with progressive paralysis gave a characteristic reaction with liquor Belostii. Stucken finds the

reaction positive in a great many diseases other than progressive paralysis and in the latter his positive findings were proportionally much lower than Butenko's. He, therefore, concludes that the reaction is without diagnostic value.

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**On the Transmission of Scarlatina to the Chimpanzee.**—LANDSTEINER, LEVADITI, and PRASEK (*Compt. rend. Soc. de biol.*, Paris, 1911, 641) have made several attempts to infect a chimpanzee with virulent matter from a child suffering from scarlatina. In their first experiment the throat of the chimpanzee was painted with material taken from the tonsils and pharynx of children suffering with scarlet fever with angina. This was followed in two days by a redness and swelling of the tonsils, fever, and presence of streptococci in the tonsillar secretions. Four days after the inoculation the throat was painted again and 75 c.c. of defibrinated blood taken from a severe case of scarlet fever were inoculated. Two days later there were redness and intense swelling of the pharynx, tonsils, and pillares of the fauces; white deposits on the tonsillar mucosa, and a general exanthem. The animal was very ill and died three days later. Abscesses formed at the point of inoculation of the blood. Autopsy: Swelling of the cervical glands and mediastinal glands; points of interstitial inflammation in the kidneys; lesions of the skin resembling those in scarlet fever. In the second case the injection of 50 c.c. of scarlatinal blood under the skin and painting of the throat as before was followed in forty-eight hours by slight fever and tonsillitis. There were no general phenomena. Reinjection ten days later produced tonsillitis again. Inoculation of streptococci isolated from the throat of these chimpanzees produced no result in the throats of others. In other words, painting the throats of the chimpanzee with products coming from scarlatinal children provokes an angina similar to that of patients suffering from scarlet fever, but it is not certain whether this angina is produced by the scarlatinal virus or by some other infection. While the observation is single and insufficient in itself, the authors point to the advisability of further experiments of the same nature.

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**Use of Urotropin in Pneumonia.**—SHATTUCK (*Bost. Med. and Surg. Jour.*, 1911, clxiv, 842) reports his experience with the routine use of urotropin in pneumonia. It was originally given as a preventative for empyema in doses of 10 grains, *t. i. d.*, but after a study of 59 cases treated with the drug, as compared to 188 not treated with it, the incidence of empyema was certainly not lowered. The hopeful feature of the treatment is the fact that no pericarditis or otitis media developed in any of the cases.

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**Antityphoid Vaccination per Rectum.**—COURMONT and ROCHAIX (*Presse Méd.*, 1911, 453) have vaccinated men per rectum against typhoid fever instead of subcutaneously. A bouillon culture of Bacillus typhosus was killed by heating to 53° C. After a preliminary evacuant enema, the patient was given 100 c.c. of this suspension of dead bacilli through a high rectal tube, 15 drops of laudanum being added to facilitate retention. The enema was retained about twenty-four hours. In no case was there fever, malaise, colic, or backache. The enemata

were repeated at the end of five and ten days. After a period of ten days the serum of the individual showed marked changes to the Bacillus typhosus. The agglutinative power had risen to 1 in 30; the bacteriolytic to 1 in 20, while the bacteriocidal power soon reached 1 in 1000. Should this method, after due trial, prove effectual, objection to antityphoid vaccination would be reduced to a minimum, for all complaint has been based upon pain in the joints and backaches, the malaise and fever incident to the first subcutaneous inoculation.

**Treatment of Diabetics with Soda Bicarbonate, Intravenously.**—Lépine and Labbe have for some time advised the treatment of diabetics in coma or showing premonitory signs with soda bicarbonate, intravenously. SICARD and SALIN (*Bull. et Mém. Soc. Méd. d. hôp. de Paris*, 1911, xxviii, 854) now advocate its use in certain diabetic conditions dissociated from coma, such as pruritus and muscle pains, but which have resisted dietetic and medicinal efforts. They have used much stronger solutions with great success, and observe that a solution of 9 or 10 per cent. in place of 1 or 3 per cent. is well borne by the patient and can be freely repeated. The solution is, of course, sterilized in a closed flask and used in amounts of 100 to 250 c.c. This represents in 100 c.c. about 10 grams, or 280 grains, of the bicarbonate. The injection is made into the veins of the arm, but the greatest care must be exercised not to get the solution into the surrounding tissues, because it is very caustic. The possibilities of such concentrated doses are much increased when one remembers that in coma or in cases showing premonitory signs, it may be necessary to use large doses of bicarbonate, and at the same time avoid raising blood pressure by injections of great volume.

**Angina Pectoris with Vasomotor Excitability.**—MACKENZIE (*Heart*, 1911, ii, 265) has observed a man, aged thirty-five years, who had rheumatic fever and syphilis. For five years he had frequent attacks of pains in the chest, with fever, nausea, and palpitation, coming on even when he was quiet. He always avoided motion and generally had a pulse of 70 to 90 per minute, and blood pressure of 130. The heart was enlarged and gave clinical evidence of aortic regurgitation and stenosis. The pain was typical in distribution to the left chest and arm. In an attack the pulse rate rose to 120 and the pressure to 240, varying directly with the severity of the pain. Following the administration of amyl nitrate, the pressure sank to 150, coincident with the cessation of pain, but pressure rose and pain returned as the effects of the drug wore off. Morphine and chloroform produced similar effects. Realizing that the nervous system was at fault, as shown by the vasoconstrictor mechanism, he was given bromides with good effect. At autopsy aortic regurgitation and hypertrophy were found, with no great involvement of the coronary arteries. The association of aortic valve disease with angina is well known, and this case presents the typical features of arterial constriction, more marked in cases of aortic valvular disease than in other forms of angina. In all forms of angina much more efficient results can be obtained by attention to the nervous system than by cardiac therapy, and bromides are ideal for such a purpose.

# SURGERY

UNDER THE CHARGE OF

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**Disinfection of the Field of Operation in Abdominal Operations.**—PROPPING (*Zentralbl. f. Chir.*, 1911, xxxviii, 661) says that the increased occurrence of mechanical obstruction since the introduction of iodine disinfection led him to question whether this use of iodine could play a causal role in the production of the obstructions. Iodine is an excellent substance with which to produce adhesions between serous surfaces. Propping established the following facts: If, a half-hour after coating the skin with iodine, a cloth moist with saline solution is laid on the browned skin for half a minute, the cloth at the area of contact will give with starch a strong iodine reaction (blue discoloration). Even when the choth touches the browned skin for only a moment, the iodine reaction can be produced, although weaker. If in an animal experiment the intestines are laid a short time on the iodine stained skin, the intestines will give the iodine reaction. One can obtain the same result in man with the extirpated appendix. The field of operation toward the end of the operation, especially when it has been handled with fluids, as saline solution, is almost always deprived of its color. This faded area will no longer give the iodine reaction. Therefore the iodine must have passed to the surrounding regions and structures. In animal experiments (on rabbits), according to R. Heinz, very small amounts of iodine injected intraperitoneally will produce in a short time abundant layers of fibrin and firm membranes and bands between the intestines. The effect is to a certain degree specific, in contrast to that of turpentine. Propping injected intraperitoneally in a dog 20 drops of the tincture of iodine, dissolved in 80 c.c. of sterile saline solution, and found after forty-eight hours, in the region of the liver and stomach, abundant fibrous adhesions. There were no adhesions in the region of the small intestines. Evidently dogs are little suited to the development of experimental adhesions, on account of the activity of their intestinal and body movements. The abdominal cavity in the human subject, on the other hand, inclines especially to adhesions, particularly from a moderately specific irritation, as from gonorrheal infection. Propping has, since the introduction of iodine disinfection, in about 70 cases of appendicitis, simple or complicated with abscess or peritonitis, 6 times found ileus from kinking or adhesions. This was unusual before the use of iodine for this purpose. Of about 300 cases of appendicitis in 1910 and 1911, before the introduction of iodine

disinfection, there were only 5 cases of mechanical intestinal obstruction. He concluded that eventration of the intestines directly upon the browned skin should be absolutely avoided. They should be laid on interposed layers of gauze moist with saline solution. Whether this will be sufficient to prevent harmful effects from the iodine must be determined by further observations.

**Cystoscopic Diagnosis of Syphilis of the Bladder.**—HABERERN (*Zentralbl. f. Chir.*, 1911, xxxviii, 663) refers to the quotation from Nietze in the scanty literature on this subject, to the effect that a syphilitic process in the bladder has not yet been established by the cystoscope. Nietze, however, believed that the future would show that, notwithstanding the older literature, the bladder was not completely immune to the virus of lues. Haberern reports the case of a woman, aged forty-one years, who had had, for fourteen years, an ulcer on the tongue, which healed very slowly under the application of caustics. At the same time she had pain in the throat and dysphagia, which lasted a long time, and since then she has been speaking with a nasal twang. Later she had similar chronic ulcers on the thigh. For four years she has been having frequent micturition, urinating during the day every three-quarters to an hour, during the night every two hours. The condition has been growing worse during the last few months. The urine is bloody at the end of micturition, which is followed by pain. Examination at the hospital showed absence of the uvula and left half of the palatoglossal arch, and several contracted scars in the throat. If the patient was placed in a somewhat bent forward position, fluid taken into the mouth passed out again from the nose. The Wassermann reaction was positive. The cystoscopic examination showed the bladder wall smooth and glistening. The openings of the ureters were normal. The wall of the sphincter was swollen and uneven, and close behind it there was a round ulcer the size of a walnut. On its left side there was a tumor, three or four points on which were tubercular and all but one covered by mucus membrane. At the most prominent part of its surface it was ulcerated and suppurating. This was diagnosticated as a gumma. An injection of Ehrlich's arsenobenzol was given. Twenty days after the injection a cystoscopic examination showed that the bladder wall was not smooth and shining as before the injection, but was hemorrhagic in places. Fine trabeculæ were visible on the lateral wall and vertex. The tumor at the sphincter was entirely smooth. Five weeks after the injection the patient was discharged from the hospital in good general condition and free of urinary disturbances. Before her discharge the cystoscope showed the swelling at the sphincter and the gumma reduced to a small smooth protuberance. The urine was almost normal.

**The Displacement Posteriorly of the Prominent Premaxillary Bone in Complicated Harelip without Drawing in the Tip of the Nose.**—REICH (*Zentralbl. f. Chir.*, 1911, xxxviii, 859) says that when the premaxillary bone is especially prominent in a double harelip, its displacement backward is accompanied by a pulling on the nasal septum and with it the tip of the nose, a pug nose being thus produced. To overcome this tendency Reich operated on a child, aged three months,

in the following manner: The profile of the nose was normal, but after dividing the vomer and pushing back the premaxillary bone into the gap in the alveolar arch, a marked deformity was produced from the pull on the tip of the nose. The stunted median portion of the lip was then separated from the premaxillary bone. An incision was made directly upward as far as possible through the mucous membrane, perichondrium, cartilaginous septum, and perpendicular plate of the ethmoid bone. The bleeding was slight. There remained along the bridge of the nose a broad piece of bone and cartilage, which maintained the existing profile of the nose, because it did not accompany the backward displacement of the premaxillary bone. In order that the mucoperiosteum of the nasal wall may not resist this backward movement it is first divided. The vomer behind the premaxillary bone is then divided subperiosteally and in a V-shape before pushing the premaxillary bone back to its proper place. The nourishment of the remaining portion of the vomer is aided by making this V-shaped excision subperiosteally, the nasopalatine artery being thus preserved. After the premaxillary bone is placed in its proper place it is fixed in position by the repair of the harelip. This should provide two short lateral incisions in the cheek, according to the method of Mirault for mobilizing the lateral flaps. The median piece of the lip which has been separated upward is employed to complete the normal septum. The result of the operation was good. There was absent the flattening due to extirpation of the premaxillary bone, which now filled the defect in the alveolar arch. The disturbance in the development in the upper jaw when the premaxillary bone is removed was not seen. The nasal septum was high, the tip of the nose not drawn in, and the profile of the nose was good.

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**Myonephropexy.**—Jiano (*Ann. d. mal. d. org. gén.-urin.*, 1911, i, 981) did the following operation for a movable kidney on the right side in a woman, aged fifty years. The patient was placed in the left lateral decubitus, with a cushion under the flank to render the right side prominent. The left lower extremity was flexed upon the abdomen and the right placed in extension. Spinal anesthesia was employed. An incision was made along the external border of the erector spinæ muscle, beginning at the lower border of the tenth rib and ending 2 cm. above the iliac crest. The incised skin was dissected on both sides from the underlying muscles for about 5 cm. An incision was then made through the first plane of muscles formed by the latissimus dorsi and the small inferior serratus. On the internal side of the wound these muscles were dissected up from the erector spinæ. From the latter were cut two muscle strips, one short and one long, and both one to two centimeters wide. Then the other muscle layers were divided and the kidney exposed. The latter was brought to the surface and decapsulated over an area of 2 cm. The isolated muscle strips were passed transversely under the kidney, as a support for the latter. The distance between the two muscle strips was from 3 to 4 cm., which allowed for the hilum of the kidney. A catgut suture was passed through the free end of each muscle strip. In the upper part of the wound, about 5 cm. from the external edge, the muscle flap is penetrated by a Reverdin needle from without inward. The needle is then threaded

with one end of the catgut suture of the first muscle strip and the suture drawn through the muscle flap. The other end is drawn through in a similar manner, a half centimeter away. Both ends being tied together, the first muscle strip is fixed, thus supporting the superior pole of the kidney. Three or four centimeters lower, the other muscle strip is fixed in a similar manner. A transverse bridge is thus formed for the support of the whole kidney. To prevent movement of the kidney, the edges of the stripped-up capsule are fixed on each side to the muscle strips. The abdominal wall is then closed with sutures. Eleven days after the operation the patient left the hospital completely cured. Jiano concludes that myonephropexy is an operation easy of performance and absolutely benign. It assures a good fixation of the kidney without any disturbance in the escape of urine. It dispenses with all inconvenient products owing to the permanence of the supports—pain, suppuration, fistulæ, and the formation of sclerotic tissue in the renal parenchyma.

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**Concerning a Case of Invagination of the Ileum Cured by Resection: A Contribution to the Treatment of Intussusception.**—Haagn (*Deut. Zschr. f. Chir.*, 1911, 142) says that the general tendency is to regard total resection as indicated only when all other methods of treatment have failed. He reports a case in which, after exposure of the intussusception which involved the ileum about a hand's breadth from the cecum, it was found impossible to reduce the invagination. It was resected and the bowel ends united by circular suture. The patient recovered and was discharged one month after the operation. Three months later the patient was again examined and found well, and six months pregnant. She was delivered successfully. Leichenstern found that in 479 cases of invagination spontaneous reduction of the invagination occurred in 15 cases; also in 15.6 per cent. of the cases of invagination of the ileum, with a mortality of 42.6 per cent. We cannot, therefore, rely upon this method of treatment. Haagn agrees with Rydigier in the following conclusions on the treatment of intussusception: In acute invagination operation should be performed as soon as possible after properly employed non-operative measures have been tried without success. When a laparotomy has been done, disinvagination is to be preferred when it can be carried out without special difficulty. If the intestinal wall at any place in the area of invagination is suspicious, a strip of iodoform gauze should be introduced to this place or the affected area excluded from the abdominal cavity. Resection of the whole invagination is indicated when the intestinal wall shows marked changes or threatens perforation. The employment of an artificial anus, or entero-anastomosis, is to be condemned. Haagn believes that in ileocecal and colon invagination, when disinvagination has been difficult and the serous surface of the intussuscipiens is intact, the intussusceptum may be resected. In case, however, the invagination is only a short one, a total resection should be done, because of the better prospects of a radical cure, although one should also take into account the general condition and age of the patient. If very short, unless reduced with very little difficulty, resection is to be preferred to all other methods. But even when the invagination is easily reduced, a secondary resection must be kept in mind, since it is the only sure means for the prevention of a recurrence.

# THERAPEUTICS

UNDER THE CHARGE OF

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**Irritation of the Kidneys by Salicylates and its Prevention by the Administration of Alkalies.**—GLAESGEN (*Münch. med. Woch.*, 1911, lviii, 1125) has found that the salicylates induce an albuminuria when given alone. The administration of from 6 to 10 grams of sodium bicarbonate in the course of twenty-four hours is sufficient to prevent this albuminuria. Thus the kidneys are saved, which may be of distinct advantage in the treatment of patients who have had a previous kidney lesion. The therapeutic action of the salicylate did not seem to be modified by the alkali. In general, twice as much of the alkali as of the salicylate was necessary to prevent this albuminuria in the cases studied by Glaesgen.

**The Treatment of Anemia with Salvarsan.**—LEEDE (*Münch. med. Woch.*, 1911, lviii, 1184) reports a case of severe anemia that closely simulated pernicious anemia in which great improvement was obtained by injections of salvarsan. Subsequently the Wassermann reaction indicated that the anemia was of luetic origin. Leede has also treated undoubted cases of pernicious anemia with absolutely no benefit. The results were fatal in 5 cases treated, although in 4 the treatment was given as the last resort. Leede thinks that if salvarsan benefits markedly any case of severe anemia, it is of diagnostic value and points to a luetic basis for the anemia.

**Fatalities after Injection of Salvarsan in Patients with Cardiovascular Disease.**—MARTIUS (*Münch. med. Woch.*, 1911, lviii, 1067) has collected 18 cases where death followed the injection of salvarsan in patients suffering from some form of cardiovascular disease. He reports the details of these fatalities, and in analyzing, them in order to ascertain the cause of death, he concludes that in only 7 cases death occurred as a result of the injection. In 5 of these 7 cases the autopsy findings showed the triad, syphilitic aorititis, sclerosis of the coronary arteries, and myocardial degeneration. In 1 case there was found myoplasia of the heart and aorta. The seventh case showed severe pathological changes in many of the organs. Four of these fatal cases showed no objective signs during life of any cardiovascular trouble. Martius concludes that syphilitic aortitis, especially if complicated with coronary arteriosclerosis or myocarditis, is an absolute contraindication to the use of salvarsan. He thinks that angina pectoris, unless associated with changes in the heart muscles, is not a contraindication, and even may be favorably influenced by the injection of salvarsan. Martius says that there is absolutely no danger in giving salvarsan by intravenous injection to patients with sound hearts and arteries, provided that the remedy is given well diluted.

**The Treatment of Pernicious Anemia.**—Effendi (*Deutsch. med. Woch.*, 1911, xxxvii, 930) relates the history of a patient suffering apparently from pernicious anemia. When first observed the red blood cells were 1,280,000; the white cells, 4800; and the hemoglobin 38 per cent. Because of the history of a previous luetic infection, active antiluetic treatment was given, but the anemia progressed. Iron and arsenic also had no effect, and the red blood cells fell to 970,000, with 20 per cent. of hemoglobin. Effendi then tried glycerin in doses of a tablespoonful three times a day, and later this dose was increased to 70 grams. The improvement was rapid, and at the end of a month the red blood cells were 4,200,000, with 100 per cent. of hemoglobin. Since then the patient has remained perfectly well, and the red blood cells have increased still further, to 5,200,000. Effendi was led to try this method of treatment by the report of a case of pernicious anemia similarly treated by Tallquist, who had equally good results. He does not think that glycerin will cure every case of pernicious anemia, but believes that it may benefit only those of intestinal origin.

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**Salvarsan in the Treatment of Malignant Tumors.**—Von Czerny and Caan (*Münch. med. Woch.*, 1911, lviii, 881) have tried salvarsan in the treatment of various malignant tumors. They found that salvarsan had a distinct beneficial effect upon inoperable malignant tumors, especially upon sarcoma when the Wassermann reaction was positive. They observed a considerable diminution in the size of sarcomatous tumors, together with an improvement in the general condition. The cases of carcinoma showed no objective signs of improvement, although marked diminution of pain and a considerable general improvement usually followed the injections. They suggest that salvarsan therapy may be of value after the surgical removal of sarcoma in order to prevent a probable recurrence. This treatment is contraindicated in cachectic and in very weak patients. They believe that it may be possible to increase the dose of salvarsan for the treatment of malignant tumors, and then better results may be obtained. Usually a single dose of from 0.4 to 0.6 gram salvarsan was given, and they question whether a number of small repeated doses of salvarsan would not have had greater therapeutic effects. The question is also raised as to the effect of local injections of salvarsan into the tumor combined with the remedy given in the usual manner.

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**The Therapeutic Use of Pituitrin.**—Klotz (*Münch. med. Woch.*, 1911, lviii, 1119) reviews the work of many different observers regarding the action of pituitrin in raising abnormally low blood pressure. From his own clinical observations and experimental work on animals, Klotz is very favorably impressed by the beneficial effects of pituitrin in conditions that are associated with lowered blood pressure. He recommends it especially in uterine hemorrhage due to postpartum atony of the uterus. He also thinks it may be of value in other hemorrhages dependent upon a low vasomotor tone and in postoperative shock, although he has no personal experience with its use in such conditions. Klotz also suggests that it should be used in conditions of low vasomotor tone due to the toxins of acute infectious diseases. He says that pituitrin has the marked advantage over adrenalin, in

that its action is more moderate but prolonged over a greater period of time. There are no untoward by-effects from its use, but he advises against giving it to patients with abnormally high blood pressure. Pituitrin may be given by mouth in doses of 0.2 gram of the fresh gland substance, or it may be obtained in a form suitable for intramuscular injection. The latter method seems to have a more certain and more rapid action.

**Some Observations Concerning Veronal.**—Von Noorden (*Therapie d. Gegenwart*, 1911, lii, 287) says that veronal is more certain in its action than most of the other hypnotics. He also believes that it is perfectly safe when given in proper dosage. A certain degree of depression, dizziness, and headache have seemed to follow the use of veronal, but von Noorden thinks that these after-effects may be ascribed to the fact that larger doses than necessary were employed. He advocates combining small doses of phenacetin with veronal. He believes that when given in such a combination, a much smaller dose is necessary for hypnotic effect and the unpleasant after-effects are avoided. Von Noorden says that 0.3 gram of veronal combined with 0.25 gram of phenacetin has the same hypnotic action as 0.6 gram of veronal when given alone. When insomnia is accompanied by cough or pain, the addition of small amounts of codeine also enhances the hypnotic action of veronal.

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**The Towns-Lambert Treatment for Morphinism and Alcoholism.**—Cabot (*Bost. Med. and Surg. Jour.*, 1911, clxiv, 76) speaks highly of the Towns-Lambert method of treating morphinism and alcoholism. He has already seen results sufficient to confirm him in the belief that, aside from suggestion and any notable psychical impressions, the treatment has great value, especially for patients with the morphine habit.

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**Iodides in High Blood Pressure and Arteriosclerosis.**—Matthew (*Edinburgh Med. Jour.*, 1911, vi, 228) believes that iodides have a noticeable effect in lowering blood pressure in patients with high blood pressure but without arteriosclerosis. He says that they are useless in increased blood pressure associated with advanced arteriosclerosis. The initial dose of potassium iodide must be 0.6 gram in order to obtain any lowering of the blood pressure, and this dose must be rapidly increased in order to secure its maximum action. Matthew thinks that the organic preparations of iodine in the ordinary therapeutic doses as given contain too little iodine to be of any value as vasodilators. They should only be given when the iodides are not well borne by the gastro-intestinal tract. The best of the organic preparations seems to be sajodin.

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**Lipanin as a Substitute for Cod-liver Oil in Rachitis.**—Schabad and Gurochowitsch (*Monats. f. Kinderheilkunde*, 1911, ix, 659) say that the action of cod-liver oil in rachitis has been theoretically explained by its rich content of free fatty acids. Acting upon this assumption, Mering has introduced to us a substitute for cod-liver oil—olive oil with the addition of 6 per cent. of free oleic acid. This may be obtained

under the trade name lipanin. The authors have investigated the therapeutic action of lipanin in rachitis especially with reference to any possible action upon the metabolism of the mineral salts, and have come to the following conclusions: (1) Lipanin as well as olive oil increases the absorption of nitrogen and of fat, but lipanin is not superior to olive oil in these respects. (2) Lipanin has no influence whatever upon the calcium metabolism in rachitis, and therefore cannot replace cod-liver oil in the treatment of rachitis.

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**The Physician's Attitude toward New Remedies.**—HEUBNER (*Therap. Monatshefte*, 1911, xxv, 402) sounds a warning regarding the overproduction of new proprietary remedies often differing but slightly in chemical structure and to which are attached names that are so entirely different that their close relationship is concealed. He gives the formulas of six very closely allied remedies as regards their chemical structure, as an example of this practice. These remedies are anesthesin, profesin, cycloform, neuronal, adalin, and bromural. Heubner says that this practice has the bad effect of burdening the memories of practising physicians with a long list of names of remedies that differ but slightly, if at all, in their physiological action. He cites other examples of this practice, such as applying the name medinal to veronal natrium. Heubner says that most of these drugs have some therapeutic action, but are not superior to the old tried remedies. Furthermore, all these new remedies lack sufficient critical trial to justify their supplanting the old remedies, and their increasing number necessarily prohibits the thorough trial of a remedy before a new modification is brought forward.

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**The Results of the Treatment of Tetanus with Subcutaneous Injections of Carbolic Acid.**—BACELLI (*Berlin. klin. Woch.*, 1911, xlviii, 1021) reviews the results obtained by a large number of different clinicians who used subcutaneous injections of carbolic acid for the treatment of tetanus. Bacelli was the first to advocate these injections for therapeutic purposes, and he makes use of a 2 or 3 per cent. solution of carbolic acid injected either subcutaneously or intravenously. He says that it is possible to give from 0.5 gram to 1 or 1.5 gram of carbolic acid to patients suffering from tetanus. These doses are divided in the course of twenty-four hours, and the urine is closely watched for possible toxic effects. Bacelli says that patients with tetanus tolerate these large doses of carbolic acid remarkably well. He gives the details of 94 cases of severe tetanus and 38 cases of very severe type treated by this method. Of the 94 severe cases only 2 per cent. died, and the mortality in the very severe cases ranged from 19 to 15 per cent. The entire number of patients treated by this method, as reported in the literature, is 190. There were 33 fatal cases in the whole series, thus giving a mortality percentage of 17.36. Bacelli says that the dose of carbolic acid given to many of those patients who succumbed was entirely too small. One of the fatal cases was due to a gangrene of the arm, following the injection of the carbolic acid. Bacelli believes that the results obtained by this method of treatment are for superior to those obtained by the therapeutic use of tetanus antitoxin.

# PEDIATRICS

UNDER THE CHARGE OF

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**The Serodiagnosis of Anterior Poliomyelitis.** — EDWARD MILLER (*Deut. med. Woch.*, 1911, xxxvii, 1105) points out that the clinical interest in the experimental immunization of apes to anterior poliomyelitis by a serum lies in the fact that this indicates the presence of antibodies in human beings who have recovered from anterior poliomyelitis, and that it makes possible a serodiagnosis of epidemic anterior poliomyelitis. The latter would be of great value, especially in the abortive form of the disease. Müller and Römer have made investigations which have convinced them that these antibodies develop also in human beings in conjunction with epidemic anterior poliomyelitis and remain in the blood for many years. Active virus from apes was mixed with the serum of an immunized human being for many hours and then injected intracerebrally in apes. Controls received in the same way virus mixed with serum from individuals who never had anterior poliomyelitis. The controls contracted the disease, while the test cases escaped, presumably because of the antibodies present in the immunizing serum. Miller examined a typical case of abortive anterior poliomyelitis. The clinical diagnosis of this form rests on the fact that in an epidemic several children in one family show identical prodromal symptoms; but one of them fails to develop the paralysis which attacks the others. Using the serum from this case in the test stated above, he found the serodiagnosis positive, thereby substantiating the clinical diagnosis and proving that this form of anterior poliomyelitis does exist. This coincides with the results obtained by Anderson Frost, who found in an epidemic 9 cases which had suspicious prodromal symptoms; but which developed no paralysis. They neutralized an emulsion of active virus six times with the blood serum of these cases. It is still a question whether the predisposition to the disease found in children is that of the spinal cord or the portal of entry. The liability of the lymphatic system to disease in children, and the hypothesis that the virus is carried to the spinal cord through the lymphatics favor the former idea, while the latter possibility has been rather neglected. Just as a positive reaction in this serodiagnosis indicates an abortive case of anterior poliomyelitis, so does a negative reaction absolutely indicate the absence of poliomyelitis infection. This fact Müller demonstrated in another series of experiments. In proof that there is no etiological difference in the sporadic and epidemic forms of the disease, Müller reports that the serum from a case which had the sporadic form six years before neutralized the virus of the epidemic form exactly the same as did the serum of the epidemic form. This serodiagnosis may well prove to be highly important in tracing the origin of widely separated local epidemics. Owing to the expense, the difficult technique, the length of time necessary, and the possibility of errors due to using unrecognized abortive

cases for controls, this method of serodiagnosis is rather applicable to the development of research work than to general practice and isolated cases. The clinical value of the method, however, is greater in children than in adults. The method would seem most valuable in recognizing sporadic cases disguised as Landry's paralysis or acute bulbar paralysis of childhood. The antibodies which have been demonstrated as early as the sixth week after infection, exist and may be found for years afterward, and this method of serodiagnosis will become of paramount importance to the pathological and histological methods of diagnosis. The therapeutic value of an antiserum in this disease has so far proved negative.

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**The Treatment of Early Infantile Paralysis by Immobilization.**—E. MAYER (*Deut. med. Woch.*, 1911, xxxvii, 1107) adds an important feature to the local treatment of the paralyzed parts in anterior poliomyelitis by describing MacKenzie's method of immobilization. Up to the present time the usual treatment of this disease has been rest in bed, hydrotherapy to combat fever, and pain and, locally, inunctions of mercury. Krause, believing the gastro-intestinal tract to be the avenue of infection, recommends calomel to disinfect the intestines. After the acute stage has passed, the paralyzed parts are usually massaged, treated by electricity, and eventually placed in splints. While some cases are cured by this treatment, yet the greater percentage are uninfluenced by it, and subsequently exhibit the most pitiful contractures and paralyses. The contractures arise from the recovery of one set of muscles without the recovery of the opposing muscle group; from long continued crooked positions of the patient in bed, or from the pressure of the bed clothing. The development of a pes equinus, for instance, can often be avoided if the foot is protected from the weight of the bedclothing. In the light of the relatively poor results from the routine treatment, the proposition of MacKenzie is highly interesting. He recommends, where paralysis occurs in the upper extremity, that the muscles, immediately on being affected, be placed at rest by splints and kept so for weeks or months. Also that the position be such as to relieve the muscle of any functional movement. By absolute rest in bed, the position and angle of the splint is gradually changed. In 10 patients coming under observation during the first ten days, MacKenzie reports 9 as being cured by this method. In 3 of the cases a good result was apparent in from four to seven weeks up to eight months of treatment, with rest in bed and splints. Five cases treated with massage and electricity for over three months showed no sign of improvement. MacKenzie believes that with his method a subsequent mechanical or surgical treatment is unnecessary. Mayer, in introducing this method, suggested its use also in the lower extremity, and the use of a plaster-of-Paris mould instead of splints. The use of plaster mould tends to prevent severe degrees of contracture and the formation of exudates. Mayer reports 2 cases in which he used the new method. One case had paralysis of the arms, legs, and back. Improvement was pronounced in four weeks. In two months the child had entirely recovered except for a slight paralysis of the tibialis anticus. Another case with one leg affected and with paralysis of the quadriceps recovered in four weeks. This method of immobilization with plaster tends to avoid reflex irritation of the spinal cord.

# OBSTETRICS

UNDER THE CHARGE OF

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**The Unfavorable Influence of Pregnancy upon Chronic Progressive Deafness.**—BRICKNER (*Amer. Jour. Obstet.*, June, 1911) finds that, although the pathological process present cannot be clearly made out, pregnancy in women suffering from chronic progressive deafness becomes a serious matter and increases the deafness. This bad effect is evident so soon as pregnancy begins, increases during gestation, and remains permanent after delivery. Repeated pregnancies make the hearing progressively worse. If pregnancy be interrupted the hearing may temporarily be better, but subsequently will deteriorate. Abortion should be induced as soon as it is evident that pregnancy is injuring the hearing. It might be justifiable, at the request of the patient, to render impregnation impossible.

**The Influence of the Automobile upon Obstetrical Conditions.**—EDGAR (*Amer. Jour. Obstet.*, June, 1911) has investigated the subject of the use of the motor car upon obstetric conditions. He believes it to be true that the motor car causes more vibration than any other vehicle; the distance traversed at one sitting is almost invaribaly greater with the motor car than with the horse-drawn vehicle, and the patient is almost unconsciously exposed to considerable strain. The effect of the motor car on the nervous and circulatory systems is very different from that produced by other vehicles. Some patients seem but little disturbed even though high speed is used and long runs are made, and minor accidents on the road may occur. Such patients can usually be allowed to use a motor car during pregnancy, if very careful to avoid actual physical fatigue, and do not use the motor at the times corresponding to the menstrual periods. Other patients are made intensely nervous and excited by the use of a motor car, with rapid pulse and often insomnia. The continuous use of the motor car tends to produce constipation, and hemorrhoids are made worse by motoring. Pelvic or abdominal congestion or inflammation is made worse. Pyelitis and appendicitis are aggravated. Displacements of the uterus and subinvolution are also made worse. If the motor car be used immediately after abortion or labor, subinvolution may be caused and backward displacements aggravated. In many anemic women, who are too flabby to take exercise, the motor car has proved a positive benefit, and in cases where prompt treatment is necessary the motor car has undoubtedly assisted in the saving of life.

**The Susceptibility of Pregnant Women to Tuberculin.**—BAR and DEVRAIGNE (*L'Obstétrique*, April, 1911) believe, from their investigations, that pregnant women have diminished sensibility to the reaction of

tuberculin. This diminution does not seem to exist during the entire period of pregnancy, but seems most pronounced during the last months of gestation.

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**Sacro-iliac Relaxation.**—MEISENBACH (*Surg., Gyn., and Obstet.*, May, 1911) has made the study, from the standpoint of orthopedic surgery, of this condition, and publishes a well-illustrated paper, with analysis of 84 cases. He concludes that the sacro-iliac joint is a true joint, normally admitting some motion. It may be subjected to strain or complete sublaxation as well as to the diseases which affect other joints. The pelvic girdle is the main support of the trunk, and when relaxed may jeopardize the sacro-iliac joint, loosening the sacrum or causing an actual dislocation. Sciatica often results from the slipping of the sacro-iliac joint, and many of the backaches from which women complain are caused by sacro-iliac strain. An habitually abnormal attitude and also flat foot in young and old, may predispose to strain of the sacro-iliac joint. The degree of motion in this joint varies greatly, and is usually more marked in walking. Strain upon these joints may be produced by a pendulous abdomen and direct or indirect muscular violence or general debility may further partial dislocation of the joint. A diagnosis should be made of this condition as early as possible, as its prompt relief may prevent distressing and prolonged nervous disturbances. In acute cases, with sharp pain and spinal curvature, early treatment may give immediate relief. All cases must not be subjected to fixation, as the success of treatment will depend upon the detection of the cause. In these cases the pelvic girdle must be supported, and thus strain upon the joints be relieved. This subject is of practical interest to the obstetrician, because relaxation in the sacro-iliac joints following labor is not uncommon. The more severe the labor, the more poorly developed and anemic the patient, the greater is the liability to this complication. Inability to walk, fatigue, indefinite pain, especially upon turning in bed or rising from a chair, are the principal symptoms. The patient will usually refer this pain to the affected region, and if she be lying upon a firm bed or table, pressure over this joint will cause pain. Sacro-iliac relaxation is a complication of considerable importance after difficult forceps deliveries and especially after symphysiotomy or pubiotomy. Cases in which the occiput rotates posteriorly in labor are more apt to be followed by this condition than is normal labor. The tretament consists in avoiding the prolongation of labor by proper instrumental delivery without delay, and by applying a well-fitting bandage about the pelvis. In performing symphysiotomy or pubiotomy, care should be taken that at the moment of delivery the two halves of the pelvis are not rotated too widely asunder.

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**The Slow Pulse of the Puerperal Period.**—LYNCH (*Surg., Gyn., and Obstet.*, May, 1911) has investigated 105 cases to determine the lessening of the pulse rate after the birth of the child. These were 103 primiparæ and 82 multiparæ. Slowing of the pulse of multiparæ occurs twice as often as in primiparous patients, in whom the pulse beat is often unchanged in the puerperal period. In six out of every ten women in the series examined the average pulse was three or four

beats slower than normal. In the total series a fall of ten or more beats was observed in 20.5 per cent., in 31.7 per cent. of the multiparæ, but in 12.7 per cent. of the primiparous women. The more rapid the pulse has been during pregnancy, the more apt is it to be slower in the puerperal period. While the slower the pulse during gestation, the more apt is it to increase in rate after the birth of the child. In the majority of cases the pulse does not rise when the patient leaves her bed, about the eighth day.

**The Relation of the Thyroid Gland to the Female Generative Organs.**—GOODALL and CONN (*Surg., Gyn., and Obstet.*, May, 1911) report cases illustrating this subject, demonstrating that a very intimate relationship exists between the female generative organs and the thyroid glands, this relationship being especially close between the thyroid and the ovaries. The uterus has no influence upon thyroid activity, except as it may affect the action of the ovaries. The function of the thyroid gland is, in a measure, under the control of ovarian activity, and when this is in excess, exophthalmic goitre often develops. When ovarian activity is diminished or absent, myxedema may result. Puberty, menstruation, pregnancy, lactation, and menopause all have a profound influence upon thyroid secretion. Thyroid and ovarian secretions neutralize each other, and the interstitial cells of the ovary are the important factors in producing this result.

**The Beginning of Mind in the Newborn.**—PETERSON (*Bull. Lying-in Hosp. of N. Y.*, December, 1910) reports the results of investigations made in the New York Lying-in Hospital to determine the degree of mentality present in the newborn infant. From these studies he concludes that sensibility to light is present in most infants at birth, even when premature. The optic nerve is ready to receive impressions before birth. The same is true of hearing, as many normal children react to sound on the first day of life, and also a considerable number of those prematurely born. Children react to stimulation of the gustatory nerve at birth, and often before the period of normal gestation. This is also true of the olfactory nerve. There is every reason to believe that cutaneous sensibility, muscular sense, sense of motion, and of position are present, not only at birth, but for some time before. Thirst hunger is experienced on the first day, although hunger for food is not usually apparent until the first or second day. There are good reasons for believing that a newborn child comes into the world with a small store of experiences and appreciated feelings and shadowy consciousness. The child's body transmits light readily and must also transmit sound, and the child must have heard *in utero* the sound of the mother's body and also its own heart beat. The gustatory nerve is stimulated by swallowing amniotic fluid. Touch and muscular sense must be developed by fetal movements, which occur as early as the sixteenth week of pregnancy, and may be so violent as to give pain to the mother. Muscular activity and frequent contact of the fetal body with the uterine walls must develop a sense of equilibrium and relation to space. The material basis of consciousness is prepared long before birth. There is no perceptible difference in the reaction of colored and white or between twins.

# GYNECOLOGY

UNDER THE CHARGE OF

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**Study of the Structure of Myomata by Means of a Myoglia Stain.**—HEIMANN (*Zentlbl. f. Gyn.*, 1911, xxxv, 701) believes that so little progress has been made in establishing a definite, characteristic structure for uterine myomata, owing to the fact that the ordinary stains used in their study, such as van Gieson, do not bring out the finer details of the muscle fibers. He calls attention to the occurrence in the smooth muscle cell of two kinds of fibrils, which according to Benda are to be considered as differentiation products of the cell body, as having, therefore, arisen from protoplasm. One set of these is finely fibrillar; they constitute the so-called "Binnenfibrillen," forming the mass of the cell body; the others, coarsely fibrillar, form the "Myoglia" of Benda, or the "Grenzfibrillen" of Heidenhain. These lie around the periphery of the cell, do not enter into it, but extend beyond the end of the cell and intertwine with corresponding fibrils of neighboring cells. By means of Benda's special myoglia stain, Heimann has found in a study of 25 small myomata, for the most part just visible to the naked eye, that in each case the muscle bundles radiate from a point, not necessarily anywhere near the centre of the tumor, which is sometimes formed by a lymph vessel, at others merely by a rich collection of muscle nuclei. He found even the smallest myomata to be made up of a number of these nodules, which structure can also be seen in quite large tumors.

**Function of the Ovary.**—In an article replete with references to the literature, as well as embodying original investigations, FRANK (*Surg., Gyn., and Obst.*, 1911, xiii, 36) discusses the present status of our knowledge of the above subject. He calls attention to the fact that several glands in the body have a dual function, for example, the hypophysis has an anterior portion which is necessary to the maintainence of life, and a posterior or "nervous" portion, which is not so; the pancreas likewise has a double action. It furnishes an external secretion from the islands of Langerhans. It is not assuming a physiological curiosity, therefore, to consider that both the ovaries and testicles have an external secretion (ova, semen), and an internal secretion affecting the sexual life of the individual. The author considers the corpus luteum the most important constituent of the ovary in the latter respect, although in certain species of animals, but not in all, the existence of an "interstitial gland" has been demonstrated. He considers that the weight of evidence shows the corpus luteum to be developed entirely from the granulosa cells of the follicles; that it is therefore an epithelial structure. It has been shown by Loeb that the persistence of the corpus luteum is of the greatest importance in pre-

paring the uterus to receive the ovum, as without a corpus luteum in the ovary no decidua can be formed in the uterus; the fertilized ovum under these conditions merely acts as a foreign body in the uterus, and cannot obtain a foothold. When, however, the ovum is once firmly attached it becomes independent, and the removal of the ovaries or corpora lutea does not necessarily interrupt the pregnancy. The presence of a corpus luteum, moreover, lengthens the sexual cycle by absolutely inhibiting further ovulation as long as it persists; pregnancy *per se* does not do this, however, as if all corpora lutea are removed after pregnancy is once established, the remaining portions of the ovaries being allowed to remain in position, ovulation may occur. The factors causing the persistence of the corpora lutea in pregnancy are not known, but the author's investigations tend to indicate that neither the fetus nor the trophoblast are the sole factors.

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**Diagnosis of Renal Calculus.**—LICHTENBERG and DIETLEN (*Münch. med. Woch.*, 1911, lviii, 1341) recommend for this purpose distending the pelvis of the kidney with oxygen, claiming several advantages for this method. Oxygen distends and renders röntgenologically visible the kidney pelvis and calices as well as does collargol, but it does not obscure the shadow of a stone as does the latter substance; it is therefore useful not only in diagnosticating the presence or absence of a stone, but also in showing its exact location, and whether it is best approachable by nephrotomy or by pyelotomy. The technique consists merely in introducing the ureteral catheter into the kidney pelvis, or high up into the ureter, and attaching its end to a tube from an ordinary oxygen tank such as is used for inhalation purposes. The pelvis becomes fully distended, the excess oxygen returning through the ureter alongside of the catheter to the bladder. The stream is kept running while the picture is being taken. No complications are to be apprehended, and the procedure is not painful.

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**Ovarian Transplantation.**—MARTIN (*Surg., Gyn., and Obst.*, 1911, xiii, 53), as a result of a very extensive review of the literature of the subject, and of his own investigations, reaches the conclusion that autotransplantation (*i.e.*, transplantation of an ovary or portion of an ovary of an individual into the body of the same individual) is a comparatively simple procedure which may be accomplished, in the majority of cases successfully, by attaching the cut surface of the graft to any well-nourished tissue, such as the parietal peritoneum, abdominal musculature, subcutaneous tissue, etc. Even a very small portion of an ovary thus successfully grafted preserves the sexuality of the individual, and prevents symptoms of a premature menopause. Heterotransplantation, transplantation of an ovary from one individual into the body of another individual, on the other hand, succeeds much less frequently, owing to the antagonism of the blood of every individual to tissues of another, this antagonism not existing between the blood and tissues of the same individual. Martin suggests the possibility in the future of preparing patients in some way so as to render the blood and tissues of donor and recipient homogeneous, and thus make heterotransplantation more uniformly successful.

# HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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**Beriberi.**—FRASER and STANTON (*Philippine Jour. of Sci.*, 1910, v, 55 to 64) have carried out a series of experiments first upon chickens, then upon human beings, which indicate definite progress along both preventive and curative lines in beriberi. Chickens were fed upon unpolished and polished rice respectively. The chickens receiving polished rice, that is, rice containing no pericarp, developed a typical peripheral neuritis in from sixty to eighty days, while control chickens fed upon unpolished rice remained healthy. The experiments were repeated with similar results. The chickens showing symptoms of neuritis were then fed upon polished rice together with rice polishings, and in many instances fully recovered. Similarly those chickens which were fed upon whole rice and which remained well upon this diet developed polyneuritis when they were fed for a corresponding period upon polished rice. Apparently the process of polishing rice removes something which is necessary in order to maintain health upon a strict rice diet. The experiments were then carried out along similar lines upon human beings, and with the same general results; that is, that those individuals fed upon polished rice developed typical symptoms of beriberi, while those receiving unpolished rice remained well.

**On the Etiology of Beriberi.**—DEHAAN (*Ibid.*, pp. 65 to 71) has come to similar conclusions as follows: (1) *A* disease described as beriberi, or polyneuritis epidemica bears a very great resemblance in its etiology, prophylaxis, and therapeutics to the polyneuritis which can be artificially produced in animals, principally in fowls. (2) Just as is the case in the latter, the former is almost always the result of eating cleaned rice; that is, rice deprived of the whole of its pericarp, although other articles of food prepared in a similar manner may also cause an outbreak of the disease. (3) The pericarp of the rice and also some parts of the grain are removed in the manipulation by which unhusked rice becomes cleaned rice. Certain constituents of the greatest importance in securing normal nutriment for the peripheral nervous system are lost during this operation. (4) The constituents are neither salts nor nucleins, and (5) their character is still unknown.

**Phosphorus Starvation with Special Reference to Beriberi.**—HANS ARON (*Ibid.*, pp. 81 to 97) has studied the amount of phosphorus both in the polished and unpolished rice, and has carried out experi-

ments somewhat similar in nature to those just mentioned. His conclusions are: (1) Food stuffs, especially rice, which are relatively poor in phosphorus (phytim), if they are the main or exclusive article of diet for any great length of time, have been shown by various authors to cause beriberi. (2) The process of polishing removes the outer layers from the rice. These are rich in phosphorus, especially soluble organic compounds of that element (phytim). They are food constituents probably of high physiological importance. (3) A diet similar to that which is regarded as the probable cause of beriberi, if exclusively given for any length of time to animals, is not sufficient to keep them in normal health. (4) Polyneuritis has been observed in chickens receiving a food similar to that which is regarded as causing beriberi, viz., white rice. The addition of organic phosphorus in the form of phytim or its salts, considerably, but not entirely, produces a deleterious effect of a diet (white rice) which can produce polyneuritis in chickens.

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**Lead Poisoning in Illinois.**—ALICE HAMILTON (*Jour. Amer. Med. Assoc.*, 1911, No. 61, pp. 1240 to 1244) calls attention to the unprogressive attitude of this country as compared with other countries, particularly those in Europe, concerning the recognition and dangers of lead poisoning. The lack of statistics and legislation in the United States for the control of the lead industries appears to be due largely to the fact that medical men have not taken the interest in the subject that the foreign medical men have, and this unprogressive attitude, it might be remarked parenthetically, is true for many other phases of the great question of occupational hygiene. The manufactures which employ the greatest number of men working in lead are those for white lead, lead smelting, the manufacture of storage batteries, printing establishments, and to a lesser extent those places where lead glazing is done. While it is well known that women are much more susceptible to lead poisoning than men, the statistics of Illinois indicate that very few women are employed in lead industries. The prevention of lead poisoning necessitates a campaign of education among those employed in the lead industries, the study of the conditions by competent investigators, the collection of statistics and presentation of statistics to legislative bodies, together with recommendations for the drafting of suitable laws regulating the manufacture of lead in factories.

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